

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010



## In This Edition

- [Message from Lynne Byers](#)
- [Rx-360 Offers New Feature](#)
- [Rx-360 Update](#)
- [A Supplier's View](#)
- [Regulatory News](#)
  - [USA](#)
  - [Europe](#)
  - [India](#)
  - [China](#)
  - [WHO](#)
- [Interesting Supply Chain News](#)
- [List of Members](#)
- [Call for Papers](#)
- [Contact Information](#)

## Rx-360 Mission:

Create a global quality system that meets the expectations of industry and regulators and helps ensure patient safety by enhancing product quality and authenticity throughout the supply chain.

## Message from Vice Chair, Lynne Byers:



When Rx-360 was first set-up, an interim board was appointed. To help with the principle that Rx-360 was global and not too US-centric, it was agreed that the chair and co-chair should come from different parts of the world. My role as Head of Supplier Quality Shared Service in GSK is a global role with me being based close to London. In my role, I am aware of the increasing difficulties we have to obtain access to suppliers and also the fact that there are few globally recognised standards for auditing pharmaceutical suppliers. One of the most important aspects of the work of Rx-360 is to adopt and agree to global audit standards. We are working with other organisations such as PQG/IPEC to adopt existing standards.

One thing which has impressed me in working with the working groups and the Board has been the energy and commitment which people have shown to move all the working groups along so quickly. I am particularly looking forward to reviewing the first Rx-360 audit performed under the pilot scheme. This is expected to be available sometime after May.



## New Features for the Rx-360 Community:

**Training Aids:** Need a training aid? Need to create a convincing argument for the need to secure the supply chain? Then Rx-360 has your answer. A series of educational videos have been added to the Rx-360 web site that can be used for these very purposes. Just [click here](#) to see what videos are available. More videos are added all the time.

**The New Issue of International Pharmaceutical Quality (IPQ)** provides a survey and analysis of the key CMC/review initiatives underway at the agency and international levels as the new decade begins and the impact of the evolving QbD/ICH Q8-10 paradigm. In cooperation with IPQ's Editor-in-Chief, Bill Paulson, Rx-360 is pleased to make the issue available to its member companies on a complimentary basis ([click here](#)).

In focus in the April IPQ issue are:

- The new ICH quality initiatives on Q8-10 implementation, drug substances, pharmacopeial methods and heavy metals.
- The progress in revamping the CMC review processes in the US and Europe to advance the new QbD paradigm, and how associations like Rx-360 and organizations like USP, EDQM, NIST and PQRI are trying to fill in the remaining gaps.
- How communication boundaries are expanding – within companies and regulatory agencies, between industry and regulators, and between agencies internationally – to accommodate the QbD approaches.

This issue's "Voices from the Dialogue" features: CDER's Christine Moore and Steven Kozlowski and EMA's Evdokia Korakianiti on implementing QbD for drug and biotech products in the U.S. and Europe, respectively; CDER's Nakissa Sadrieh on regulating nanotechnology in therapeutics; and Genentech's Christa Hartmann on a new knowledge management paradigm.

The May IPQ will provide a companion analysis of how the inspection and GMP enforcement components of the regulatory picture are being impacted as the quality system foundation for continuous improvement strengthens.

The IPQ staff and Rx-360 hope you enjoy the new IPQ issue. Please visit the IPQ web site at [www.ipqpubs.com](http://www.ipqpubs.com).

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

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## Rx-360 Update:

Rx-360 continues to make progress on developing an appropriate and effective process to share supplier audits and conduct joint audits. As outlined below, the Consortium is taking steps to implement pilot programs which will provide the organization information to assess feasibility, effectiveness, and potential gaps and areas of improvement for shared supplier audits and joint audits.

**The Audit Sharing Working Group** has initiated the Rx-360 Audit Sharing Pilot (to share existing audit reports). All member suppliers have been contacted and the Working Group has conveyed to these companies the relevant agreements, process, and background information. The Working Group has also contacted non-member suppliers and is actively following up with these companies.

**The Auditor Qualification Working Group** refined minimum qualification requirements for third-party auditors to conduct Rx-360 Joint Audits and opened online auditor registration sites and started the selection process for the Pilot.

**The Audit Standards Working Group** has finalized an Rx-360 API Guideline and a Supply Chain Security Checklist for use as a supplement with other standards in all Rx-360 audits. The Working Group is also (i) developing an Rx-360 Basic/Chemicals and Raw Materials Guideline and Checklist; and (ii) reviewing the IPEC/PQG Draft Excipients Guideline for purposes of developing an Rx-360 Excipients Guideline and Checklist.

**The Audit Design Working Group** has finalized all forms and templates needed for the Joint Rx-360 Audit Program and conducted member surveys to identify suppliers of APIs, excipients and raw materials/basic chemicals - from North America, Europe and Asia (including India, China and Japan - as candidates for the Joint Audit Pilot program).

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

**The Audit Database Working Group** is reviewing a new software extranet option for managing the pilot audit reports and other related materials. The Working Group is also developing a long-term plan for the post-pilot audit database.

**The Quality Management System (QMS) Working Group** has held coordinating teleconferences with all Rx-360 Audit Program Working Group leaders. The Working Group has also developed an Audit Program Management Table listing key deliverables and timelines for all Rx-360 audit program working groups. The Working Group has prepared a high-level QMS describing the key aspects of the proof-of-concept pilots for the Rx-360 Auditing Program and Audit Sharing Program. In addition, the Working Group has prepared drafts of a Quality Policy, an Ethics/values statement, a training approach (with associated documents) for auditors, and a framework for evaluating the pilot programs.

In parallel with all of its audit-related work, Rx-360 continues to actively monitor and share with its members updates on relevant regulatory and legislative developments, and current events regarding pharmaceutical quality. The Consortium is committed to external outreach and continues to update the pharmaceutical, supply chain and regulatory communities with information on its activities.

Organizations interested in becoming an Rx-360 Member or Observer should contact the Rx-360 Secretariat at [Rx-360@dbr.com](mailto:Rx-360@dbr.com).

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## Rx-360: A Supplier's View:

Audit Sharing Will Improve Supply Chain Efficiency & Safety

By Tom Beil, Vice President, Quality & Regulatory Affairs,  
Sigma-Aldrich / SAFC

Sigma-Aldrich / SAFC is a global organization with 31 manufacturing sites in 11 countries. As both a leading industry supplier and customer we see multiple benefits in the Rx-360 consortium and are pleased to participate in its Audit Sharing Program, which has been designed to create greater supply chain transparency and improve efficiency.

As a complete pipeline partner for pharmaceutical and biopharmaceutical companies, we currently undertake in excess of 200 customer audits each year, in addition to our standard FDA and EMEA audits, and see standardization of the



# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

audit process and the sharing of audit information as ways to significantly reduce both the time and cost burden, while maintaining audit standards. As a customer, we carry out audits of our suppliers and, like all companies, want to utilize our internal resources more efficiently and maximize our return on investment, while enhancing the integrity of our supply chain. While we consider each of our customers to be special and unique, our vast experience has told us that their audit requirements are often very similar.

What we hope to achieve through our participation in Rx-360 is to implement a degree of standardization so that the audit process becomes more cost effective, while maintaining or improving quality in a logical fashion. Throughout SAFC we receive thousands of requests for information and, while the lists of questions that customers send for audits aren't always the same, there is a basis of consistency among them. There is currently no structure that lets us efficiently disseminate our information back to the customers so one of our goals is standardize and harmonize procedures, to make that process much more transparent and efficient.

## **The Rx-360 Standards Working Group**

One of the sub-committees within Rx-360 that we sit on is focused on the standardization of audits and auditors and earlier this year we announced the launch of the Rx-360 pilot program to share existing sponsor audits (the "Audit Sharing Pilot").

One of the functions of the sub-committee, and Rx-360 as a whole, is to both teach and share, pulling out the essential aspects of an audit and putting that into a "here's what we need to do" list.

Typically, on a three to four-day audit, the first few days are focused on the basics, such as the purity of water, the training, etc., which have to be undertaken before we can get to the more critical issues. When devising the audit sharing process, the sub-committee's thinking was that we should capture that information and leverage what we already know. From SAFC's point of view, as a supplier we would save on fewer audits and the time it takes to host them, while as a producer we would save by being a part of a consortium that can do 100 audits for the same cost in money or time that it would take my staff to do 20-30 audits.

## **The Audit Sharing Pilot Program**

The Rx-360 audit sharing process has been designed to make available the wealth of supplier audit information that already exists within consortium member companies and the purpose of the initial pilot program is to determine the value to Rx-360 members of sharing existing audits, and the effectiveness of the audit sharing process. The pilot program aims to collect audit reports and responses associated with 36 suppliers in several regions of the world -- North America, Europe, China, and India. The Working Group has sent initial communications to these suppliers inviting them to participate in the pilot program and has been following-up with each supplier in recent weeks to confirm participation and discuss questions.

**The work of the Audit Standards Working Group** is split into several sub-groups, as there are a wide variety of standards which are required. The Audit Standards Working Group and its sub-groups consist of 27 participants from 19 different companies and organizations. There are six sub-groups: APIs, Excipients, Supply Chain Security, Basic Chemicals, Packaging and Print. Of these sub-groups the first four are active and standards are being finalised. Wherever possible, existing standards are being adopted and Rx360 is working closely with other organisations. For example, PQG/IPEC are in the process of updating the excipients standards.

The standards will be used in a pilot to prove the whole auditing process. The current thinking is that a minimum of three standards will be used within the pilot programme. These are likely to be: API, Excipients and Basic Chemicals, in conjunction with the Supply Chain Security checklist, which is to be used alongside all of the other standards.

## **Collaboration key to success**

As an industry we need to recognize that spending an inordinate amount of time gathering the same information a hundred different ways, is not helpful or efficient. Similarly, if we have a hundred different customers auditing a single location, while 99 other facilities go unaudited, that's not helping anybody either. Rx-360 is about not stepping away from your responsibilities, but being able to leverage and share information among companies. Safety is not supposed to be a competitive advantage- it is what we all have to achieve, and we have to achieve it together. By working collaboratively, we will get more data and richer data, in a more efficient manner, to make better decisions.

## Regulatory News United States:

### **FDA Urges Industry to Take Additional Steps to Prevent Cargo Theft**

The U.S. Food and Drug Administration sent a letter to companies detailing the agency's concern over cargo and warehouse thefts. In its letter, the FDA seeks to:

- raise awareness among industry about each firm's responsibility to review and strengthen their security practices
- inform industry of the actions the FDA will take when the agency becomes aware of a large-scale theft, and outlines steps that firms should take; and
- emphasize the importance of notifying and informing members of the supply chain and the public after thefts occur.

The agency believes prevention of cargo theft is critical. To help achieve that goal, the FDA will continue to work closely with manufacturers and wholesalers to find ways to better secure the nation's supply chain. [Read more....](#)

### **Despite law, drug safety still a concern at FDA (Reuters)**

FDA officials say more work is needed to address lingering concerns about drug risks, including contaminated medications, counterfeit pills and other safety issues. (Reuters, March 10, 2010) [Read more...](#)

**US House of Representatives Committee on Energy and Commerce, Subcommittee on Health held a hearing on March 10, 2010 entitled "Drug Safety: An Update from FDA".** Joshua Sharfstein, Principal Deputy Commissioner of the FDA testified. [Read more...](#)

### **FDA Guidance on Standards for Securing the Drug Supply Chain – Standardized Numerical Identification for Prescription Drug Packages:**

FDA took many industry comments into account, modifying the draft guidance which, published in January 2009. The guidance addresses Standardized Numerical Identifications for package level identification, provides flexibility in the type of data carrier, does not require incorporation of either batch number or expiry and is compatible with the GS1 GTIN and AI-21 standards. For additional detail please see:

[Click here](#) to read FDA Guidance

[Click here](#) to read Rx-360 Summary of FDA Guidance

## Regulatory News European Union:

### **Czech Republic: Customs Officials Intercept Counterfeit Lifestyle Drugs.**

According to Czech customs, officials have seized over 5000 tablets of counterfeit drugs for treating lifestyle performance issues. The intercepted parcel originated in India and is the largest consignment of this kind in several years, General Customs Directorate spokesman Jiri Bartak announced this week. The counterfeits were discovered at a post office in Prague and were being sent to a Czech recipient. Customs officers seized some 7500 pieces of counterfeit medicines all last year and some 914 since January of this year. (*Prague Daily Monitor*, March 25, 2010); [Read more...](#)

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## Regulatory News India:

### **India: Officials Strengthen Action against Counterfeit Drug Makers**

In an effort to eliminate illegal drug trade across Tamil Nadu, India, Chief Minister Karunanidhi instructed senior health and police officials to take severe action against those involved in the manufacture and distribution of expired and counterfeit drugs. The push comes following the demise of a three-year-old girl after she consumed an expired drug. Manufacturing and trading in substandard and counterfeit drugs continue to pose a major threat to public health, and Karunanidhi expressed the urgent need to raise public awareness on the issue. (*The Med Guru*, March 24, 2010); [Read more...](#)

### **India asks WHO to stay away from counterfeit issues**

India has asked the World Health Organization (WHO) to confine itself to its public health mandate and not associate with the attempts to redefine “counterfeit” medicines. (*Business Standard*, May 5, 2010); [Read more...](#)

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## Regulatory News China:

SFDA official arrested in rabies vaccine scandal

An official working for the Chinese State Food and Drug Administration (SFDA) has been arrested in connection with an ongoing investigation into the adulteration of thousands of doses of rabies vaccine.

Chinese newspaper the 21st Century Business Herald reports that the official, named as Wei Liang and said to work for the SFDA's Drug Registration Department, has been charged with taking bribes of around \$145,000. (*AFP*, April 7, 2010);

[Read more...](#)

### Chinese flour adulterated with pulverised lime

Pulverised lime is being added to bleaching agents used in Chinese flour in a bid to cut production costs and boost profits, China state media has reported this week.

It is believed that some bleaching agents widely used in flour production contain as much as 30 percent pulverised lime, an inedible substance that has been linked to health problems, said China Daily (*Decisionsnewsmedia*, April 9, 2010);

[Read more ...](#)

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## Regulatory News World Health Organization

The World Health Organization (WHO) has published a draft guideline for comment, entitled Guideline for the Production and Control of Specified Starting Materials.

This guideline includes an extensive introduction section which provides both background and context for the information on "specified starting materials". WHO defines these materials as any substance which is primarily or mainly used as a starting material for the production of an API, but which itself could be used directly as an API.

[Click here](#) for the WHO Guidance Document

[Click here](#) for the Rx-360 Summary of the WHO Guidance Document

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

## Interesting Supply Chain News:

**Event: Last Mile Pharmaceutical Recovery, Date: April 28, 2010, Location: St. Louis, Missouri**

**Description:** A FreightWatch device was used in the recovery of pharmaceutical product and apprehension of the suspect from a last mile delivery location, on Wednesday, April 28. The pill bottle embedded device was observed reporting outside of the facility, prompting management to investigate the location of the device. The suspected was subsequently discovered and arrested by local police with 100% recovery of the stolen product.

### **Anti-counterfeiter sees collaborating regulators, public naming/shaming**

Drug counterfeiting is "the perfect crime," said Guy Villax of Portuguese API developer and manufacturer Hovione. "The patient swallows the weapon and is unaware of the crime." "Falsified medication is a bigger business than narcotics," Villax said in a presentation at Interphex. But in 24 out of 27 European countries, the crime is no more serious than trademark infringement on t-shirts. Sanctions need to be tougher, he said. (*Fierce Pharma*, April 21, 2010) [Read more ...](#)

### **US and Europe At Risk from Substandard Medicines**

A new report by the Stockholm Network, *Keeping Medicines Safe* cites examples and case studies from China, India, Brazil, Argentina and Turkey to demonstrate the lethal effects that counterfeit and substandard drugs can have on public health. (*PharmTech Talk*, March 3, 2010) [Read more...](#)

### **US: Baltimore Used as Waypoint in Counterfeit Trade**

An international counterfeiting ring smuggled tens of millions of dollars worth of fake Coach handbags, Nike sneakers, Gucci shoes and Cartier watches into the United States through the Port of Baltimore, federal authorities charged Friday in announcing the indictment of the ring's members. Authorities said the ring planned to expand to counterfeit drugs next. (*The Washington Post*, March 19, 2010) [Read more...](#)

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

## **Yahoo Fails to Address Counterfeit Drugs in Remarks to FDA**

At the end of February, the Partnership for Safe Medicines (PSM) answered the U.S. Food and Drug Administration's (FDA) call for comments on their docket concerning [the Promotion of FDA-Regulated Medical Products Using the Internet and Social Media Tools](#). However, Yahoo failed to address advertisers using Yahoo's service to peddle counterfeit and illicit medical products. A recent investigation of [Yahoo and Microsoft's online drug advertising](#) found that 80-90 percent of reviewed ads from drug sellers did not require a prescription or were acting unlawfully. (*The Gazette*, March 4, 2010) [Read more...](#)

## **EFPIA published the results of their product verification system pilot project.**

The pilot, held in Sweden between September 2009 and January 2010, successfully demonstrated that a product verification system at the point of dispense, based on a two-dimensional data matrix, is both robust and effective.

The pilot project scanned and verified almost 100,000 packs in 25 pharmacies across Stockholm, at the time of dispensing, in collaboration with pharmaceutical retail chain Apoteket AB. The project also had the support of pharmaceutical distributors Tamro and KD Pharma and the cooperation of LIF, the Swedish pharmaceutical manufacturers' association. Packs from 14 manufacturers were provided with the 2-D data matrix, allowing each pack to be individually identified. The EFPIA solution could provide a valuable asset in reducing the risk of counterfeit medicines reaching patients via the legitimate supply chain.

Key findings from the pilot include that the system provides for the effective identification of fake packs as well as expired or short dated packs and recalled products. There was a clear need for packs to have only a single barcode; users were sometimes confused by the presence of more than one code on the pack. The results strongly indicate that the proposed EFPIA model is viable, proportionate, secure and cost-effective.

EFPIA has sought the support of all stakeholders, which means effectively addressing their needs. Imposing high-end or expensive solutions throughout the supply chain without the close collaboration with stakeholders is likely to generate resistance to uptake. This pilot project has provided an excellent example of constructive co-operation amongst all stakeholders in the pharmaceutical supply chain; wholesalers, retail pharmacists and the authorities.

The Joint Final Report is available for [download here](#).

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

## List of Members:

### Biopharmaceutical Manufacturers

Abbott Laboratories, Alcon Laboratories, Amgen, Amylin, AstraZeneca, Baxter, Bristol-Myers Squibb, Cephalon, Eli Lilly, GlaxoSmithKline, Hospira, Johnson & Johnson, Merck & Co., Inc., Novartis, Pfizer, Sanofi-Aventis, Takeda, Watson

### Suppliers

Archimica, BASF, Fagron, Freight Watch, GE Healthcare, Hovione, Mallinckrodt Baker, Merck KGaA, Reliable Biopharmaceutical, Sigma Aldrich, Temptime, VWR, West Pharmaceutical Services

### Observers

Active Pharmaceutical Ingredients Committee, European Generic Medicines Association, European Fine Chemicals Group, International Pharmaceutical Excipients Council, Parenteral Drug Association, Pharmaceutical Services Corporation, Regulatory Compliance Associates, RMC Pharmaceutical Solutions Incorporated, SQA Services, Inc.

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## Rx-360 Call for Papers to Sharing Best Practices

Have you implemented new ideas and practices that better secure your material supply chains?

If so, Rx-360 wants to hear from you and help strengthen supply chains across industry.

The need for securing the supply chain is clear. Rx-360 was founded in 2008 on the tenet that working collectively allows us to be better able to assure patient safety. And one of the ways Rx-360 has committed to doing this is through adopting standards and best practices across industry.

To do this, Rx-360 is putting out a call for papers that share practices and ideas to secure the supply chain. With this call for papers and sharing of practices and ideas across the industry, Rx-360 aims to accelerate the adoption of best practices and our progress toward positively affecting the security of the supply chain in the pharmaceutical industry.

# Rx-360 Newsletter

Volume 2010, Issue 2

March – April, 2010

In the past two years, much effort has been put into securing the supply chain by individual companies. Through this call for papers, Rx-360 will gather practices and ideas so that they can be shared and implemented broadly across the industry. Papers will be published on the Rx-360 website and in our newsletter. Individuals can submit their papers requesting anonymity if desired.

Please send your papers to [Rx-360@dbr.com](mailto:Rx-360@dbr.com).

**Interested in submitting an article or commentary in the forthcoming Rx-360 Newsletters?**

If so, e-mail:

[Rx-360@dbr.com](mailto:Rx-360@dbr.com)

## CONTACT INFORMATION:

For further information, analysis or a briefing on any of the topics covered in this newsletter or related regulatory issues, please contact:

[Rx-360@dbr.com](mailto:Rx-360@dbr.com)

## Interested in a Company Membership?

contact: [Rx-360@dbr.com](mailto:Rx-360@dbr.com)

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