# Compliance Newsletter

## IDS Scheer Consulting – Pharmaceuticals & Life Sciences

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Welcome to a new year of compliance and industry news. Last year, the starting theme was the ongoing restructuring of the healthcare industry, which is a response to governmental cost cutting for healthcare in the western countries. The development of the Asian markets for established industrial players should be a theme to explore this year. The new Chinese Tort Law will be mentioned in this issue. As far as global compliance goes, the Warning Letters on the FDA site is probably still the best place to read the current environment. In this issue, I will call your attention to the global noncompliance problems at Novartis.

### Tort Liability in China

No one should expect that there is a level playing field for drug manufacturers or suppliers in China, and western firms should by now be aware of the new rules defined by the Chinese Tort Liability Law, which became effective in July 2010. In the past July online issue of the ISPE's Pharmaceutical Engineering, L. Su reviewed the liabilities of drug and device manufacturers and distributors in China. Besides general liabilities for suppliers of health care in China, the Tort Liability Law is especially dedicated to this industry.

A tort liability is created when a defective product causes harm to an individual. This can arise when the product has been counterfeited, adulterated, or when an adverse reaction to the treatment is associated with a previously unrecognized risk. There is no liability when the potential risk is clearly identified on the packaging. Patients can sue for damages, and the drug or device manufacturer has a special "no fault" position. That means the manufacturer may share in the liability, even when it is not at fault. The burden of proof in litigation rests upon the defendant. The manufacturer or distributor must prove that either the defect did not exist when the product was released for distribution, or that "science and technology at the time the drug was put into circulation"

was incapable of detecting the defect. Injuries caused by Traditional Chinese Medicine are explicitly excluded from tort liability.

Punitive damages are allowed with the law. L. Su recommends foreign players to carefully select their distributors in China and to establish an effective recall management in the country. Also, disclaimers on packaging need to reflect the latest knowledge of therapeutic risks, and instructions must avoid misinterpretation by patients, (idiot proof). A copy of the article is available upon request.

## Novartis faces Import Ban

Three drug manufacturing sites belonging to Novartis were recently inspected, and all were cited in a recent WL. If anything this WL illustrates the current relationship between the industry and the FDA. For example, "It is apparent that Novartis International AG (Novartis) is not implementing global and sustainable corrective actions." The old strategy of forcing the big players to set good GMP examples has failed with Novartis. It has become a contentious relationship.

The FDA found flawed and incomplete validation studies and unreported quality defects. Most observations were repeat violations, which places Novartis in the list of noncompliant firms. For example, inadequate cleaning of process equipment is a recurrent issue at its Colorado site. Cleaning must be revalidated when such issues arise.

Crystallization in an injectable drug is a serious issue, which resulted in a number of customer complaints. Yet, Sandoz Canada did not report it to the FDA (FAR report) and has relied upon visual inspection to remove problem vials. Rejection rates approaching 50% demonstrate poor process capability, a hallmark of the industry.

The outcome of this WL is an import ban from the Canadian plant and a general halt to drug approval applications and export certificates. Seizures of goods are also threatened for the 2 US locations. Further, a recent press release announced the closure of a Nebraska plant and drug recalls (not mentioned in this WL) after another recent FDA inspection.

## Other Warning Letters of Interest

German-based Osmed GmbH is also facing an import ban. It was promoting its tissue expanders for general use in the US, although they are licensed for a very narrow

therapeutic application. The FDA came and inspected them, and found numerous gaps to the Quality System Regulation (21CFR 820).

Look at the WL to autoclave manufacturer Midmark regarding expectations upon CAPA and deviation handling at a medical device manufacturer. Their CAPA system was cited because not all quality relevant data are included in analyses, particularly device failures after the warranty period. No statistical analysis was applied in reviews, and CAPA's were closed without confirming effectiveness of actions. Unless you have no quality problems, you need significant experienced staffing to keep the FDA satisfied with your CAPA system. As is typical for a supplier to the industry, Midmark also did not seem aware that it must file MDRs (medical device reports). For an autoclave, blowout of the door during steam sterilization is a MDR-reportable event.

The WL sent to global player, Akzo Nobel Chemicals, illustrates GMP concerns at an API (active pharmaceutical ingredient) manufacturer, i.e. product contamination and investigations. To the credit of the Mexican staff, the quality problems were duly recorded, but it appears that nothing was done about the black particle problem or the frequent leakage of hydraulic oil.

They also have a problem with their materials management system (SAP?). They cannot quarantine lots, and have shipped rejected lots. This reminds me of the SAP batch status feature; only unrestricted batches can be moved. Do they keep the batch unrestricted, so that they can move it? They claim that changes require approval at the corporate level, (which is apparently far away).

Clinical research, (within the US), is heavily dependent upon FDA approval, and the WL to the IRB, Bay Regional, shows that the FDA can apply a lot of pressure. This IRB has 3 documented poor inspection outcomes. Effectively immediately, this IRB is going to have trouble doing anything more than closing studies. Oversight of clinical studies outside of the US is much less intrusive; hence the growth in off-shore studies.

Sincerely Yours

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