Out with the old…
Compounding has been the foundation of the pharmacy profession for centuries. According to the Professional compounding Centers of America (PCCA), Pharmacy compounding is the art and science of preparing personalized medications for patients. Compounded medications are “made from scratch” – individual ingredients are mixed together in the exact strength and dosage form required by the patient.

Before mass produced drugs became the norm, almost all medications were compounded by a seasoned pharmacist. The modern age of pharmacy compounding, however, gave rise to the pharmaceutical industry and with it came increased governmental regulation surrounding manufacturing, distribution and branding of drugs.

In the United States, pharmacies are typically regulated by individual State Boards of Pharmacy. Pharmacies that compound medications per physician’s order have generally fallen into the gray area with little or no regulatory compliance. The Pharmacy Compounding Accreditation Board (PCAB) sets national standards for these facilities, however this accreditation is not mandatory and site inspections are lax, occurring every three years.

The FDA had been vocal in its quest for more authority and oversight of sterile compounding pharmacies. Increased demand for outsourced sterile preparation services prompted some pharmacies to compound drugs in ‘batches,’ further blurring the lines between drug dispensing and manufacturing standards. Though the FDA maintained absolute authority over drug manufacturers, it did not have the jurisdiction to step in where state authorities prevailed.

After many months of debate over who had authority over sterile compounding pharmacies, the issue came to a head in 2012 after an outbreak of fungal meningitis from a series of major lapses in quality at a Massachusetts-based compounding pharmacy, the New England Compounding Center (NECC). The news sent ripples through the compounding community. This contamination incident, though not an isolated event, killed 64 people and injuring 751 others across 19 states, setting the stage for Congress to intervene and for the FDA to claim broader powers to regulate the industry.

On November 27, 2013 President Obama signed the Drug Quality and Security Act (DQSA) legislation which set forth important provisions relating to the oversight of compounding of human drugs. Just three days later, the FDA released a series of compounding guidelines in an attempt to clarify who is being regulated and how it planned to implement the new legislation.

In with the new…
With the DQSA, Congress amended the current laws governing traditional compounding of the Federal Food, Drug and Cosmetic Act (FDCA) by proposing two very important measures towards regulating the compounding industry:

- Title 1- Compounding Quality Act: Expands and supports the FDA’s role in overseeing compounding pharmacies.
- Title II- Drug Supply Chain Security Act- An electronic track and trace program for prescription drugs in the supply chain.

For the purpose of this article, we will focus on Title 1- Compounding Quality Act and its implications to the compounding industry.

Section 503A- Title 1 of the DQSA removes certain advertising provisions from Section 503A of the FDCA which were deemed unconstitutional by an earlier Supreme Court ruling in 2002 (Thompson v. Western States Med. Ctr., 535 U.S. 357). What this
does is effectively reinstates a safe harbor for traditional compounding and removes any uncertainty regarding the validity of Section 503A. A drug is exempt from the provisions of federal law and will remain under state oversight as long as it is:

i. compounded for an individual patient,
ii. based on a valid prescription from a licensed individual physician,
iii. in compliance with US Pharmacopoeia standards and/or other FDA bulk drug substances,
iv. or ingredients that either comply with USP chapters on sterile vs. non-sterile compounding
v. or use ingredients withdrawn from the market due to safety reasons
vi. is not an exact copy of a commercially available drug
vii. subject to inspection by the FDA is not in compliance with USP chapters on compounding

Section 503B- The new law offers non-traditional compounders a pathway towards regulatory compliance by creating a new Section 503B under the FDCA for “Outsourcing Facilities.” This allows the FDA what it has always wanted… greater authority for dealing with pharmacies that operate beyond 503A. Pharmacies that engage in ‘bulk or batch’ compounding of sterile drugs will be subject to inspection based on the risk they pose. However, some “Outsourcing Facilities” might qualify for exempt status, otherwise imposed on conventional pharmaceutical manufacturers, if:

i. they voluntarily register with the FDA and become authorized by the Agency
ii. operate under the “direct supervision of a licensed pharmacist”
iii. provide a list to the FDA of drugs that they intend to compound, whether sterile or bulk in the next year
iv. refrain from compounding an exact copy of a commercially available drug unless it is on a drug shortage list
v. provide the FDA with a unique facility identifier for each of their location
vi. follow labeling standards set forth by the FDA

In addition, the FDA will also develop and maintain a current list of drug substances which may or may not be compounded, including a list of active and inactive ingredients, bulk drug substance list and drug shortage list, creating an unprecedented library of resource.

In July of 2014, the FDA issued a proposed rule that would include 25 additional products to the list of drugs that may not be legally compounded under statutory exemptions to the FDCA because these products have been withdrawn from the market because they were found to be unsafe or ineffective since FDA last published a final rule regarding the list in 1999.

On with the good…

One of the lessons learned from the NECC tragedy was the lack of communication between the FDA and the individual State Boards of Pharmacies. The new law encourages the FDA to engage with the USP, State Boards of Pharmacy and other local entities and receive ongoing reports concerning actions taken against certain compounding pharmacies. Recently, several states, including Massachusetts & Nevada have unveiled plans to increase its oversight on sterile compounding pharmacies. It will take a combined effort from both State and Federal authorities to effectively regulate outsourcing facilities that compound across state lines.

While the FDA continues to proactively increase its inspections of compounding pharmacies, whether it can effectively enforce the new law still remains to be seen. Out of the estimated 3,000 sterile compounding pharmacies in the US only about 67 had registered with the FDA as of November, 2014. And, it is still unclear if a FDA registration will actually override state board requirements. From the flood of inspections conducted in 2014, 74 sites received safety violations, leaving many within the industry questioning the overall effectiveness of the FDA.

The compounding industry is undergoing a major upheaval. It has always been the opinion of Pro-Praxis that all great changes are preceded by chaos. If patient safety is the ultimate goal, then all compounding facilities must be held fully
accountable to appropriate quality measures agreed to by the industry. The elective approach can only succeed if hospitals, physicians and other stakeholders deliberately choose to align with FDA-registered outsourcing facilities. The FDA and State Boards must cooperate to facilitate a joint plan for overseeing those facilities that have not complied with the new law. All compounding facilities, regardless of size, must be accredited by the PCAB with regular inspections performed every 2 years. While the insurance industry cannot force an outsourcing facility to register with the FDA or be accredited by the PCAB, it can offer added incentives to those which have voluntarily complied. Together, we can help forge a trail towards increased patient safety and improved quality standards for the compounding industry.

Resources:
http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/default.htm