FDA Update 2018

Rae Brown, M.D., FAAP

Chair, FDA Advisory Committee on Analgesics

and Anesthetic Drug Products


FDA
U.S Food and Drug Administration

Conflicts

- I have no financial conflicts and will not be discussing the off label use of drugs
- The opinions expressed in this presentation are mine only and do not reflect the opinions or the policy of the Food and Drug Administration, the Department of Health and Human Services, or the American Academy of Pediatrics

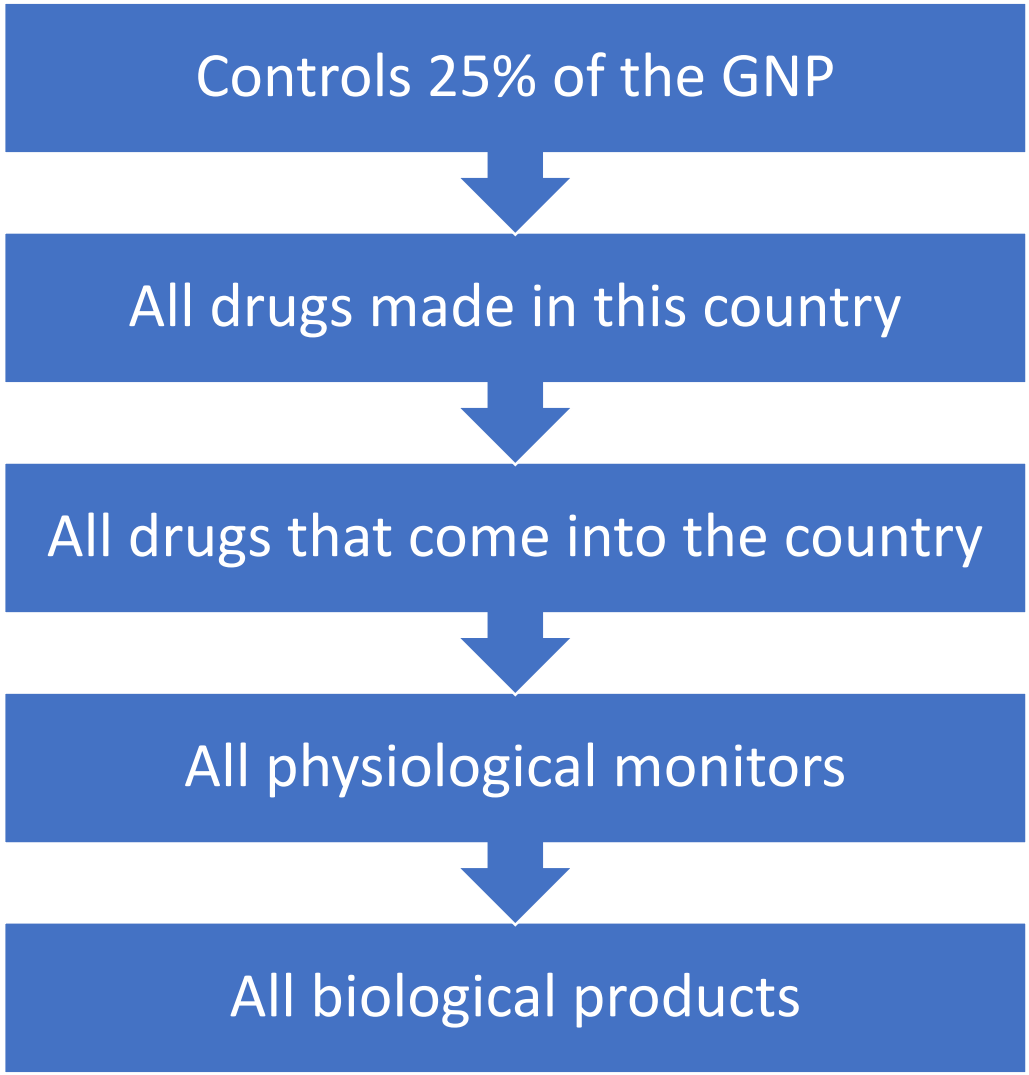
Objectives

Inform	Inform conference attendees about the depth and breadth of the responsibilities of FDA
Focus on	Focus on areas of responsibility important to the practice of Anesthesiology
Suggest	Suggest some of the current problems for the Agency that may affect future practice

The FDA and Anesthesiology

- Think about everything that you use every day.
- The FDA regulates all of it – monitors, drugs, apps.
- Most important government entity for our profession
- Some would argue that CMS is more important
- Important that they get it right

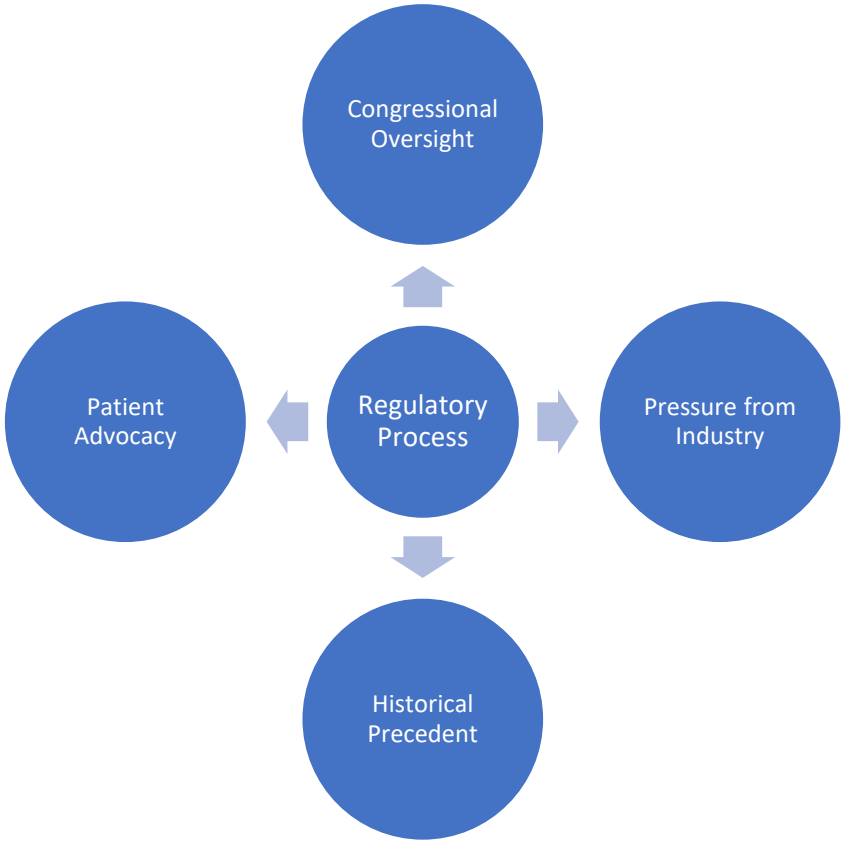
Power of the Agency



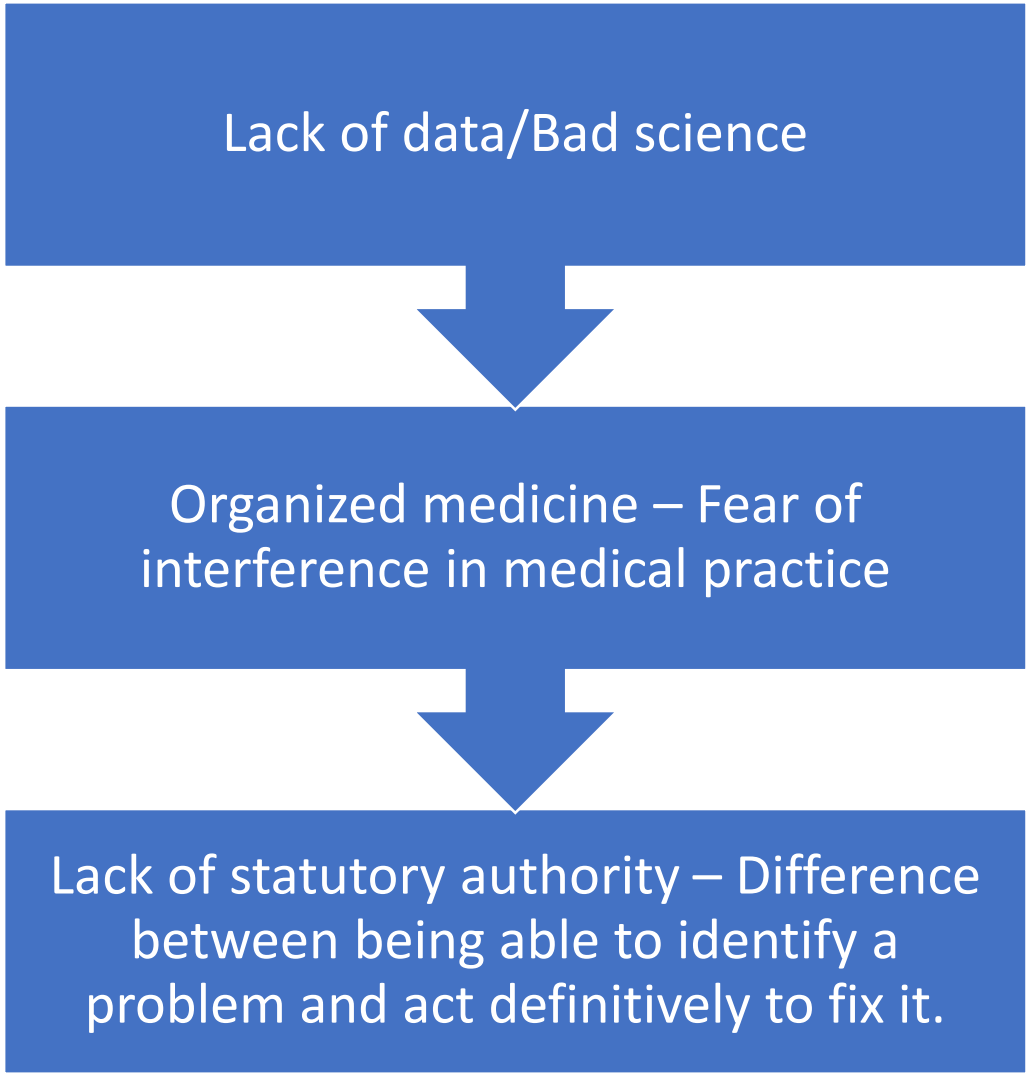
Problem

- Much of what the Agency does and many of the decisions that they make are confidential.
- The thought process for decision making is obscure, sometimes never understood.
- An Example: Zohydro - a hydrocodone formulation approved after AC vote against
- Zohydro has no abuse deterrent properties and was a rapid release formulation

Pressures on the FDA and on the General Public Health



Other Pressures



Current Issues of Importance to the Practice of Anesthesiology

2018 and Beyond

Anesthetic Neurotoxicity

General Anesthetic Agents produce accelerated neuronal apoptosis in the developing brains of all animal models.

Associated with developmental delay in memory, learning and executive function

Suggestion of some effect in humans

Why are we just figuring this out?

General Anesthetic Agents

Not tested prior to marketing in models of the developing nervous system

No post marketing testing program done for thirty years to assure safety in large populations

Point One

- The testing of all drugs marketed for human consumption must be complete and must reflect all of the clinical conditions under which the drug will be used.

Point Two

- The premarket evaluation of every drug is incomplete.
- It is only after substantial use in large populations post-marketing that we can have a complete understanding of the safety and efficacy in a diverse group of patients.

Opioid Regulation

- Opioid regulation is a major role of the Agency
- Approves labeling of compounds which can drive clinicians to use an opioid for a particular process – chronic pain
- Capable of creating new formulations by requiring industry to respond – Abuse deterrent formulations
- Organizational structure does not consider secondary consequences of opaque decision making process.

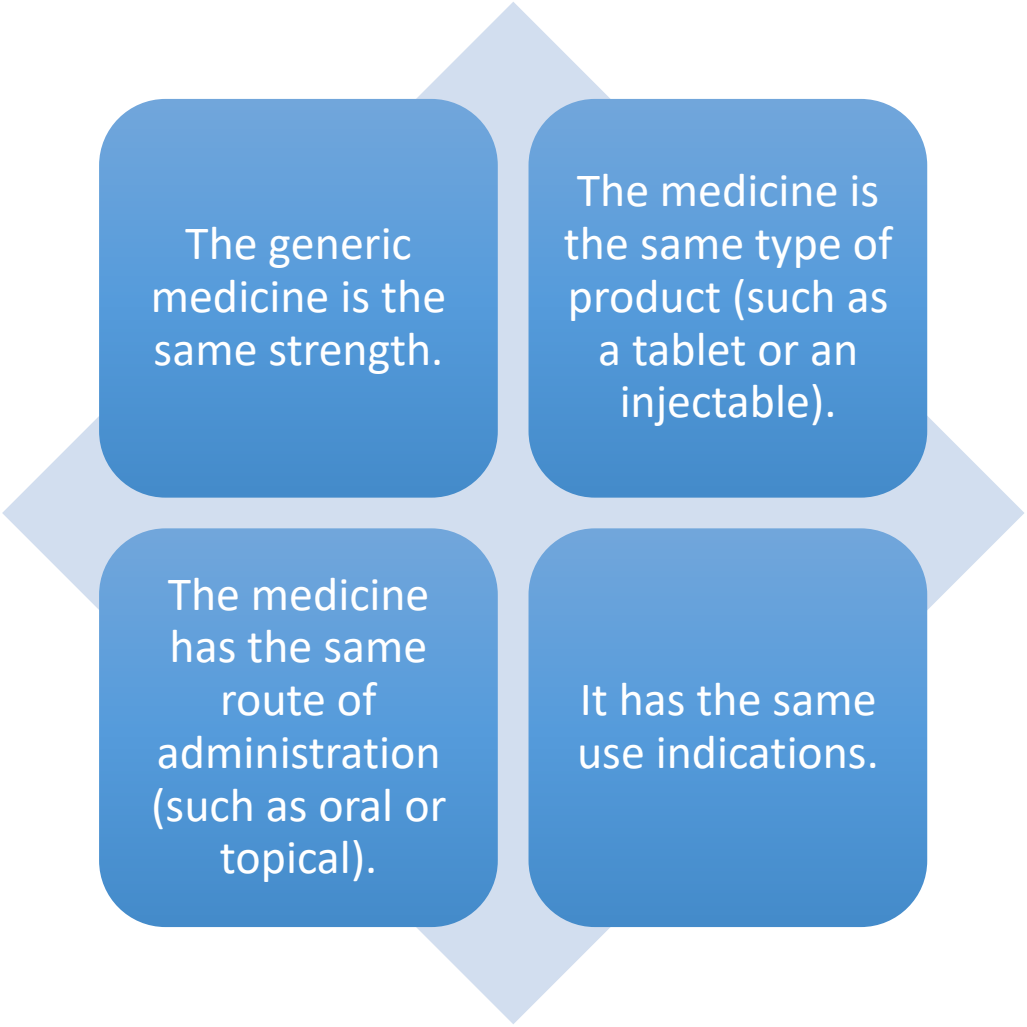
Point Three

- No system of governance, where secrecy is a defining characteristic, can be expected to provide consistent, rational answers to difficult questions.
- The insular nature of large government organizations focuses on protecting past mistakes from future review and changing the method of analysis in the near term.

Generic Medications

Important to our practice.

Generic Drugs – The FDA Standard



Generic Drugs – The FDA Standard

- The inactive ingredients of the medicine are acceptable.
- It lasts for at least the same amount of time.
- It is manufactured under the same strict standards as the brand-name medicine.
- The container in which the medicine will be shipped and sold is appropriate.
- The label is the same as the brand-name medicine's label.

Generic Drugs

- The 90% confidence intervals of the geometric mean test/reference (T/R) ratios for the above five Cmax and AUC metrics (Cmax, AUC0-T1, AUCT1-T2, AUCT2-T3, AUC0-∞) should fall **within the limits of 80.00-125.00%.**

So Generics will be similar, but often not the same

Why Focus on These Issues?

The FDA makes decisions daily that affect our patients and our profession.

It is important that we know that the decision making process is rational and impartial.

The safety of all patients depends on the Agency

We must be able to trust that they are doing the right thing every time.

At this point, I am not certain.

Summary

- The Food and Drug Administration was created to protect the public health
- The safety of pharmaceuticals must be unquestioned.
- The process of assuring the safety of drugs must be above repute.

Drug Shortages

- Industry is not required to create and market a product that will not be profitable
- The review of drugs coming from outside of the country is expensive and requires direct
- Once a drug is generic, the profit margin drops substantially
- All of the drugs that are in short supply are generic

Point-Four

- The Agency has fifteen thousand employees and a budget of 5.4 billion dollars.
- However, the statutory authority of the Agency fails to allow leadership to make substantial changes rapidly.
- Agency cannot lobby Congress.