Biopharma Product in Crisis: An Interactive Case Study

NOVEMBER 8, 2018

MINI-SUMMIT XXV
19TH ANNUAL PHARMACEUTICAL
AND MEDICAL DEVICE COMPLIANCE CONGRESS

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Disclaimer

This Product in Crisis program presents a hypothetical that incorporates various fictitious companies, individuals, products and scenarios. Any resemblance to actual companies, individuals, products or scenarios is unintentional. No aspect of this program should be deemed to reflect the position of any company or individual, or a waiver or admission in any respect.

Critical Pharmaceuticals

- 1000 employees and $1 billion in revenue worldwide.
  - Based in New Jersey
  - U.S. market represents the majority of the company's revenue
  - The company has only a basic compliance program, and the CFO is also the Chief Compliance Officer
- Primary therapeutic areas of focus include lung diseases and anemia.
  - Key product for revenue growth is Osteon, which treats chronic obstructive pulmonary disease (COPD)

Osteon® (osteonium)

- On patent / $40,000/year for treatment
- Indicated for treatment of COPD, but at least 30% of prescriptions are for other lung disease patients
- Largely a Medicare population
- In addition to a sales force, the company contracts with a leading third-party nursing educator network that provides extensive physician and patient support services

Osteon®

- The Osteon label includes a black box warning (BBW) relating to a risk of suicidal ideation and suicide
  - The BBW is based on 5 cases of suicidal ideation and 1 suicide in the course of the Osteon clinical trials

Osteon® (cont'd.)

- Osteon sales have not been meeting projections and the revenue pressures on the company have been intense
  - The VP of Marketing blames the Black Box Warning as a major drag on sales
- The Board has been threatening to sell the company if revenue targets are not met

“Osteon 2.0”

- In order to address lagging sales of Osteon, the VP of Marketing initiated “Osteon 2.0” to essentially re-launch the product
- A key component of Osteon 2.0 is equipping the sales force and nurse educators with materials and talking points intended to put the black box warning “in context”

"Osteon 2.0"

- "Osteon 2.0" was originally described in a high-level strategy deck, and it consists of the following:
  - Dissemination of a "Case Series Analysis" of the suicide and suicidal ideation cases in the Osteon clinical studies, which emphasizes the multi-factorial nature of suicide and suicidal ideation, and the presence of many such non-drug factors in the patients in the Osteon pivotal trials suffering such events
  - Funding and publishing a real-world evidence analysis of suicide/suicidal ideation in the COPD patient population, which indicates that background rates of such events in that patient population are greater than previously estimated, and concludes that the BBW on certain products for COPD patients is likely unnecessary and should not be an impediment to prescribing
  - Directing the sales force and nurse educators to provide a presentation to HCPs, their office staff and payors that emphasizes the above
    - The presentation does not disclose that the above analyses were funded by Critical

"Osteon 2.0"

- On an investor call, Critical's CEO notes that the Black Box Warning has been a serious impediment to product growth, but cites "new data, including a major analysis of a large body of real world evidence that provides compelling evidence that there is no link whatsoever between Osteon and suicidal ideation or suicide"
  - The company's stock goes up 20%
- Over the next year, Osteon sales show a marked increase, and the stock remains on the upswing
  - It appears that Osteon 2.0 is working


U.S. FOOD & DRUG ADMINISTRATION

Center for Drug Evaluation and Research
Silver Spring, MD 20993-0002

WARNING LETTER

VIA UNITED PARCEL SERVICE
SIGNATURE REQUIRED

- One year after the launch of Osteon 2.0, FDA sends very strongly worded Warning Letter to Critical – citing misbranding of the product due to counter-detailing the Black Box Warning
- Based on several Bad Ad Program complaints

Critical Convenes a Crisis Team

The Company Investigation…

- A rapid internal company investigation is conducted (consisting of 5 interviews), and it concludes that Osteon 2.0 was really the brain child of the VP of Marketing, and he had improperly pressured Medical and Regulatory to approve materials without proper support, balance, transparency, etc.
  - The CEO was aware of some of their reservations about Osteon 2.0, but says he was told it was ultimately approved by Medical and Regulatory and it "wasn't high risk"
- The VP of Marketing is fired
- The company responds to the Warning Letter within 15 business days, blaming the former VP of Marketing and proffering a corrective action plan consisting of a one-time detailing visit to each HCP office, focused on the BBW

FDA Safety Alert

- Two weeks later, FDA issues a Safety Alert based on a re-analysis of adverse event reports
  - Suggests that the prevalence of suicidal ideation among Osteon patients is actually higher than originally thought, and patients should be monitored even after discontinuing Osteon
- FDA orders a broad corrective action plan, and the imposition of a REMS
  - Prescribers must be trained on the BBW and certified to prescribe
    - Patients must join a registry and sign a patient agreement indicating that they have been educated on signs of suicidal ideation

Suicidal Ideation and Suicide in Patients Treated with Osteonium

Issue: An FDA reanalysis of FAERS reports pertaining to patients treated with osteonium (proprietary name OSTEON) suggests a higher than anticipated incidence of suicidal ideation, indicating that enhanced monitoring is necessary to ensure that physicians and patients…

Criminal Investigation

- FDA's Office of Criminal Investigation and the Department of Justice initiate an investigation
  - Expansive subpoena
  - They ask to interview key personnel at Critical

Bad Documents

- In preparing for the interviews, emails found by Critical's outside counsel suggest that company concerns about the FDA promotional risk were very clearly expressed to the CEO, even after approval by Medical and Regulatory

To: → CJones@criticalpharma.com¶
Cc: → DHaggerty@criticalpharma.com¶
From: → MNabors@criticalpharma.com¶
Date: → January 12, 2017¶
RE: → Osteon 2.0¶
¶
Charles,¶
¶
I approved the plan given the circumstances, but I think we need to be very careful about our approach to the black box warning. FDA will not be pleased if we are seen as undermining the warning, even if we believe it is scientifically dubious. Can we discuss?¶
¶
Marie¶
¶
¶
Marie Nabors, MD, PhD¶
Chief Medical Officer¶
Critical Pharma¶
¶
¶

Bad Documents (cont'd.)

- About two years ago, Critical's Chief Medical Officer and VP of Regulatory had demanded resources, citing huge problems in the company's pharmacovigilance function, including a backlog of reports and faulty coding of events
  - Her emails express a concern that events relating to suicidal ideation may be among those that went unreported
  - She received about 10% of the funds she requested

The Media

Up Next

July 14, 2019

Osteon – **Killer Drug?**

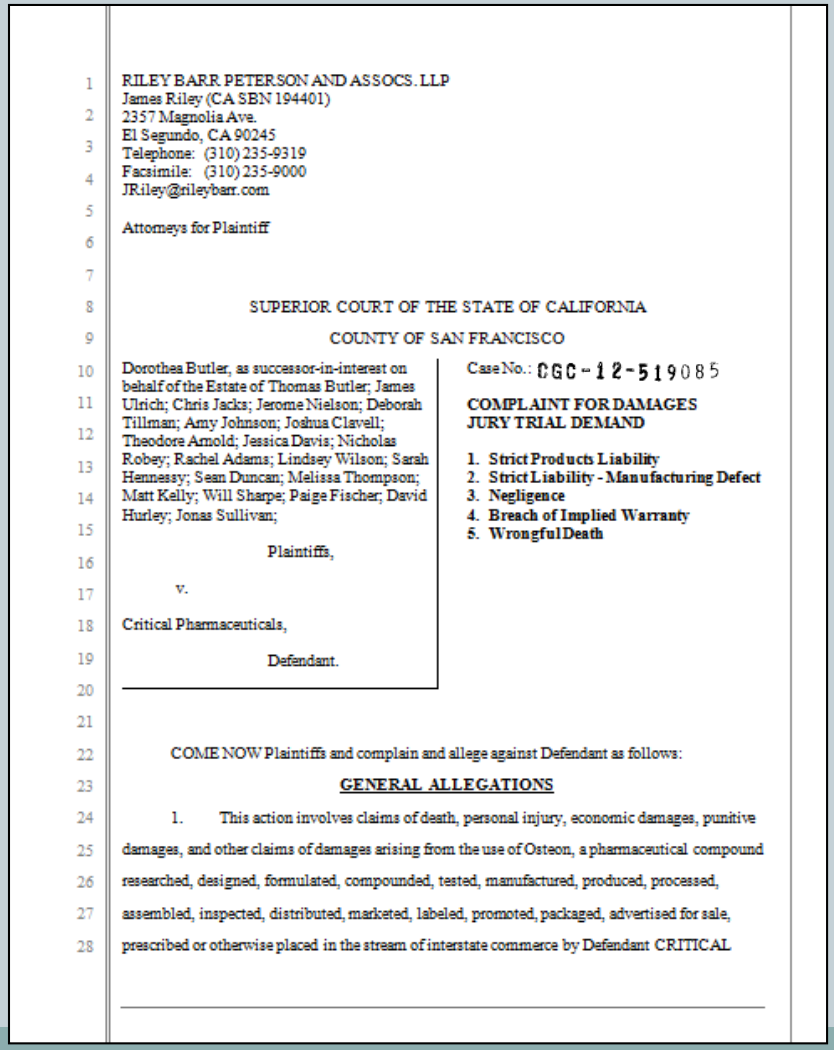
What did Critical Pharma do when it learned of patients committing suicide while taking their drug Osteon? They covered it up! A former Critical Pharma employee blows the whistle on this major scandal threatening patients across the country

Social Media Erupts

The Plaintiffs' Bar Jumps In…

Plaintiffs File Product Liability Actions

- Plaintiffs' lawyers file multi-plaintiff complaints in state court in southern Illinois and San Francisco, California



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JRiley@rileybarr.com

Attorneys for Plaintiff

SUPERIOR COURT OF THE STATE OF CALIFORNIA

COUNTY OF SAN FRANCISCO

Dorothea Butler, as successor-in-interest on behalf of the Estate of Thomas Butler; James Ulrich; Chris Jacks; Jerome Nielson; Deborah Tillman; Amy Johnson; Joshua Clavell; Theodore Arnold; Jessica Davis; Nicholas Robey; Rachel Adams; Lindsey Wilson; Sarah Hennessy; Sean Duncan; Melissa Thompson; Matt Kelly; Will Sharpe; Paige Fischer; David Hurley; Jonas Sullivan;

Plaintiffs,

v.

Critical Pharmaceuticals,

Defendant.

Case No.: CGC-12-519085

COMPLAINT FOR DAMAGES
JURY TRIAL DEMAND

1. **Strict Products Liability**
2. **Strict Liability - Manufacturing Defect**
3. **Negligence**
4. **Breach of Implied Warranty**
5. **Wrongful Death**

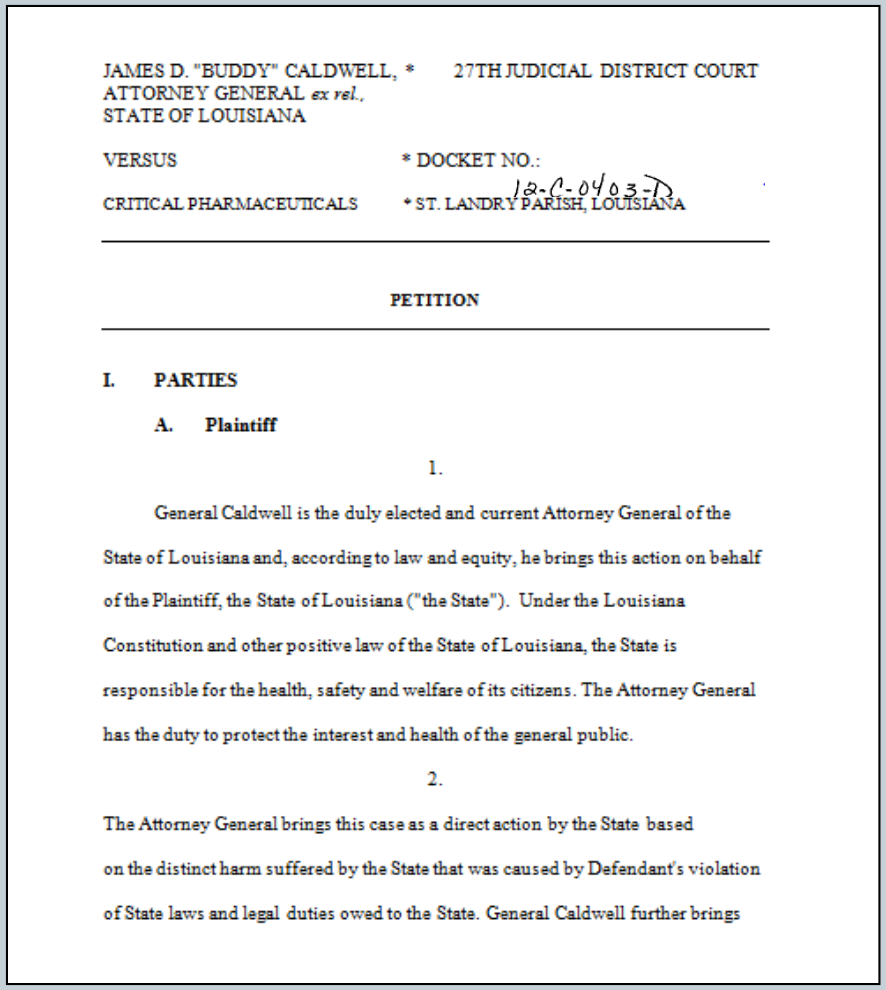
COME NOW Plaintiffs and complain and allege against Defendant as follows:

GENERAL ALLEGATIONS

1. This action involves claims of death, personal injury, economic damages, punitive damages, and other claims of damages arising from the use of Osteon, a pharmaceutical compound researched, designed, formulated, compounded, tested, manufactured, produced, processed, assembled, inspected, distributed, marketed, labeled, promoted, packaged, advertised for sale, prescribed or otherwise placed in the stream of interstate commerce by Defendant CRITICAL

Louisiana AG Files Action

- The same plaintiffs' counsel convinces the LA AG to file a *parens patriae* action in state court seeking civil penalties, restitution and injunctive relief
- LA AG hires plaintiffs' counsel under a contingency fee arrangement



JAMES D. "BUDDY" CALDWELL, * 27TH JUDICIAL DISTRICT COURT
ATTORNEY GENERAL *ex rel.*,
STATE OF LOUISIANA

VERSUS * DOCKET NO.:

CRITICAL PHARMACEUTICALS * ST. LANDRY PARISH, LOUISIANA 18-C-0403-D

PETITION

I. PARTIES

A. Plaintiff

1.

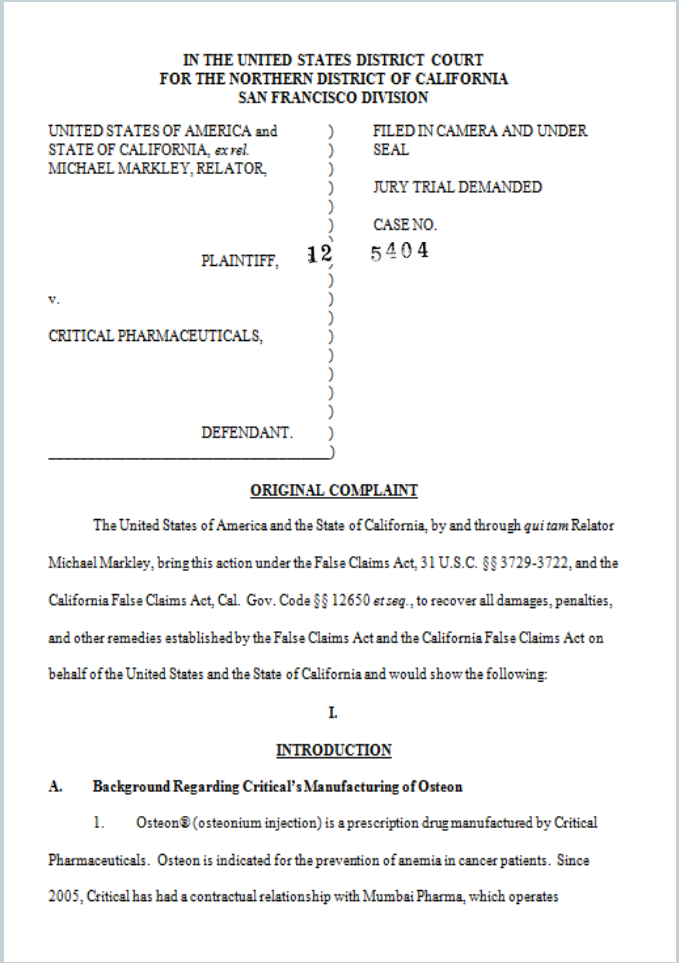
General Caldwell is the duly elected and current Attorney General of the State of Louisiana and, according to law and equity, he brings this action on behalf of the Plaintiff, the State of Louisiana ("the State"). Under the Louisiana Constitution and other positive law of the State of Louisiana, the State is responsible for the health, safety and welfare of its citizens. The Attorney General has the duty to protect the interest and health of the general public.

2.

The Attorney General brings this case as a direct action by the State based on the distinct harm suffered by the State that was caused by Defendant's violation of State laws and legal duties owed to the State. General Caldwell further brings

Qui Tam Suit Emerges

- The same plaintiffs' lawyer represents a relator and files a *qui tam* action



IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF CALIFORNIA
SAN FRANCISCO DIVISION

UNITED STATES OF AMERICA and STATE OF CALIFORNIA, *ex rel.* MICHAEL MARKLEY, RELATOR,

PLAINTIFF,

v.

CRITICAL PHARMACEUTICALS,

DEFENDANT.

FILED IN CAMERA AND UNDER SEAL

JURY TRIAL DEMANDED

CASE NO. 12 5404

ORIGINAL COMPLAINT

The United States of America and the State of California, by and through *qui tam* Relator Michael Markley, bring this action under the False Claims Act, 31 U.S.C. §§ 3729-3722, and the California False Claims Act, Cal. Gov. Code §§ 12650 *et seq.*, to recover all damages, penalties, and other remedies established by the False Claims Act and the California False Claims Act on behalf of the United States and the State of California and would show the following:

I.

INTRODUCTION

A. Background Regarding Critical's Manufacturing of Osteon

1. Osteon® (osteonium injection) is a prescription drug manufactured by Critical Pharmaceuticals. Osteon is indicated for the prevention of anemia in cancer patients. Since 2005, Critical has had a contractual relationship with Mumbai Pharma, which operates

A Congressional Subpoena Arrives…

SUBPOENA

BY AUTHORITY OF THE HOUSE OF REPRESENTATIVES OF THE CONGRESS OF THE UNITED STATES OF AMERICA

To Jason Kelly

You are hereby commanded to be and appear before the Committee on the Judiciary

of the House of Representatives of the United States at the place, date and time specified below.

☑ **to testify** touching matters of inquiry committed to said committee or subcommittee; and you are not to depart without leave of said committee or subcommittee.

Place of testimony: at transcribed deposition pursuant to H. Res. 5 (111th Cong) at 2138 Rayburn Bld

Date: February 23, 2013 Time: 10:00 a.m.

☐ **to produce the things identified on the attached schedule** touching matters of inquiry committed to said committee or subcommittee; and you are not to depart without leave of said committee or subcommittee.

Place of production: _____

Date: _____ Time: _____

To US Marshals or any authorized staff member of the Committee on the Judiciary

_____ to serve and make return.

Witness my hand and the seal of the House of Representatives of the United States, at the city of Washington, this 13th day of February, 2013.

Attest: Lorraine C. Miller
Clerk

John Conyers
Chairman or Authorized Member

A Congressional Hearing Is Scheduled…

Resolution? Settlement?

Repairing Relationships After the Crisis

- What should be done in terms of outreach to FDA, patient groups, Congress, and other stakeholders?

Key Take-Aways From the Osteon Crisis?

Thank You!