

## Vioxx Litigation Revisited: A Primer for the Paralegal involved in Case Development

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Paralegals need to ready themselves to participate in the screening of another group of claimants, who now qualify for the Vioxx® litigation, as a result of information acquired when Merck & Company released more data to the FDA in May 2006. Merck is the pharmaceutical company that aggressively marketed Vioxx® to the American public, even though it had little proven efficacy to the average person who would be using it, while it carried significant risks for causing a myocardial infarction or stroke. Paralegals need to have an understanding of the pharmacologic effects of Vioxx and the abnormal clotting that has caused such problems, along with the pathophysiology of cardiovascular disease and risk factors predisposing to thrombotic events. This article aims to provide a foundation for the paralegal involved in client screening and intake.

### **A BRIEF HISTORY**

The story starts in 1996, when in one of Merck's preclinical studies, patients taking Vioxx® (*generic name: rofecoxib*) experienced a higher rate of cardiovascular events than patient taking placebo. In spite of these concerning findings, Vioxx went on the market in 1997. In 1998 and 1999 two more internal Merck studies showed much higher risk for cardiovascular events in Vioxx users. Yet another study, the 1999 Vioxx

Gastrointestinal Outcomes Research (VIGOR) showed that Vioxx-users had almost double the risk for suffering thrombotic events, like myocardial infarction and stroke<sup>i</sup>.

Unfortunately, it wasn't until 5 years later and possibly hundreds of thousands of Vioxx-related injuries and deaths later, that Vioxx was withdrawn from the market<sup>ii</sup>. It was taken off the market after the release of the results of a study called the APPROVe trial (Adenomatous Polyp Prevention on Vioxx), which initially, in November, 2004, reported a two-fold increase in cardiovascular toxicity, after *18 months* of use<sup>iii</sup>. This drug was deemed "cardiotoxic" and "defective," but far too late.

Now, nearly two years later, Merck has revealed that the initial data released from the APPROVe study wasn't complete, and the information that was late in coming, wasn't exactly good news for Merck, because it would qualify countless additional Vioxx users as claimants in litigation against this pharmaceutical giant. The previously unreleased information showed that short term Vioxx users were also at risk for suffering cardiovascular events; in fact their serious risk for suffering thrombotic events started only days after the initiation of Vioxx use, and the risk continued for a year after discontinuing the drug! Merck now reports that some patients using Vioxx® had their first myocardial infarction (MI) shortly after achieving a therapeutic blood level of Vioxx, i.e., within six to thirteen days (with a median of *nine days*) after starting the drug<sup>iv</sup>. The newly released data also demonstrate that the very significant risks from Vioxx persist even one year after the patients stop taking the drug.

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In early May 2006 when National Public Radio (NPR) initially released this information exchanged in a “confidential” report from Merck to the FDA, they reported that “Vioxx patients were 74 percent more likely to develop heart problems in the year after they went off the drug. In the years of taking Vioxx, they were at 90 percent higher risk of heart problems.”<sup>v</sup> Cardiologists and clinical trial experts who have analyzed this data feel that the persistent risk of cardiovascular problems suggests that Vioxx does long-lasting damage to the arteries.

Merck still contends that the data does not show that the patients remained at an increased risk for hypercoagulability after the drug was discontinued.

### **MECHANISM OF ACTION**

While aspirin acts by inhibiting platelet production, causing vasodilation, and as a result, preventing thrombosis; Vioxx does the opposite. Vioxx (and other drugs in its class called “Cox-2 inhibitors”) causes platelet clumping and vasoconstriction, and as a result, promotes clot formation. Both aspirin and Vioxx work by affecting the complex chemicals called prostaglandins that are released when the body suffers an injury. In order to make prostaglandins, the body releases an enzyme called Cyclooxygenase. There are two forms of Cyclooxygenase that balance each other out. They are Cyclooxygenase-1 (Cox-1) and Cyclooxygenase -2 (Cox-2). Under normal circumstances, if Cox-2 production is stimulated, it results in a series of events that block clotting, (vasodilation, decreased platelet aggregation and decreases vascular smooth muscle proliferation). When Cox-1 is stimulated, it has an opposite effect, i.e., it causes

vasoconstriction, increases platelet aggregation, and increases vascular smooth muscle proliferation<sup>vi</sup>.

When Vioxx *inhibits* Cox-2, the equation becomes unbalanced, because Cox-1 enzymes continue to act, unopposed. The unopposed enzyme, Cox-1, acts in a manner that promotes clotting. Hence the patients who are a high risk for clotting due to pre-existing plaque in their arteries from arteriosclerotic disease are placed at an even higher risk for clotting when they are on Vioxx. Patients who are on hormones or on other drugs or are suffering from disease conditions that place them at risk for clotting (e.g., cancers, clotting disorders), are at even greater risk for a thrombotic event when they take Vioxx. Immobilized patients, patients with heart failure or other conditions causing sluggish blood flow, which places them at risk for developing clots even without Vioxx, are placed in even more danger when they take Vioxx. Even people with no pre-existing or no identifiable risk factors have nearly twice the incidence of thrombotic events when they took Vioxx.

One of the goals of the paralegal performing the intake interview and data collection is to identify and document the Vioxx-user's risk factors for clotting and co-morbidities that may have contributed to the thrombotic injury, so that the experts can evaluate whether Vioxx caused or contributed to the injury claimed.

#### **LEGAL IMPLICATIONS:**

Many more patients than originally estimated may have suffered thrombotic events as a result of their Vioxx use. Both short term users and those who suffered events in the year following discontinuance of Vioxx may now be included as claimants as a result of this new data release. Still, entry criterion for Vioxx claimants is far from standardized.

Barry Hill of West Virginia, who has over 500 Vioxx heart attack and stroke cases filed, or on their way to being filed as lawsuits, cast a wide net in his initial screening, and performed organized data collection<sup>vii</sup>. As a result of his advanced planning, as this new data becomes available, he can review his data bases to find additional claimants, rather than going back to re-interview hundreds of Vioxx-users, to determine who may now qualify. He and the other plaintiffs' lawyers, with whom he is working, believed, even before this recent data release, that *four days* of continuous Vioxx use immediately before a heart attack or stroke was long enough to increase the risk and contribute to causing the event. (They based their client intake criterion on data analysis done by Harvard cardiologist John Markis, MD, soon after Vioxx was removed from the market.)

But not all law firms used the same initial entry criteria, nor did they or do they now, use standardized interviews or intake forms. Many law firms were not set up to do the meticulous screening or data entry needed to keep up with the evolving rules in this litigation. Paralegals working with law firms involved in Vioxx litigation will have to review all past applicants' data, or re-interview Vioxx users, to determine which of them, may now qualify as claimants. They will also have to revise data collection tools, so that

information from new claimants can be properly considered and stored for re-review if and when new iterations of the entry criterion evolve.

## **CASE INVESTIGATION AND DEVELOPMENT**

So how does a paralegal get up to speed to step in on this assembly line already in motion? Unquestionably, the paralegal who presents with a sound knowledge base of the involved pathophysiology and the drug's mechanism of action will be able to perform intake interviews and data collection more effectively. Working side-by-side with a cardiac nurse to develop a good interview style and data collection tool at the outset would be optimal, however many paralegals are left to their own devices to develop a process. The paralegal, before touching his or her first Vioxx case, at a very minimum, should read nursing textbooks and nursing journal articles to gain a baseline understanding of cardiovascular disease, risk factors, and clotting disorders and on performing a cardiovascular assessment.

Attempting to gain this knowledge base by reading physician's texts tends to be frustrating because they often provides more information than a legal professional needs or wants to know. Likewise, trying to get a foundation via the internet research is not a very efficient means to the end, since the focus of articles available tends not to be specific to the paralegal's needs. For example, upon entering the search terms "cardiovascular assessment," the first several hits provide unhelpful information (at least for these purposes). These internet hits give information on interpreting heart sounds, pulses, jugular vein distention and invasive monitoring, but fail to give the step by step

overview that would give insights into devising questions for an interview as a nursing text would. A carefully constructed plan for intake questioning implemented from the beginning of client intake will save countless hours later and nursing literature tends to give practical information that is most helpful.

Following is a brief overview of the arduous task of screening and collecting meaningful data for developing Vioxx cases:

### **Data Collection**

Once the plan for data to be collected has been laid out, defining the means for storing the data is in order. The software, whether it is Word tables, Excel spreadsheets, or CaseMap timelines, is not as important as the quality of data collected and consistency of data entry. Most efficiently, data should be entered directly into the data base, as it is obtained during the interview.

### **Initial Intake**

The paralegals for the plaintiff have the benefit and the burden of eliciting medical historical information directly from the patient or his representative, before delving into the medical records. Many firms started by providing potential clients with questionnaires. Others found that skilled interviewers who could alter the intake questioning to meet the needs of the client and his case scenario, so was more efficient in both screening and in collecting meaningful data.

Each potential claimant's case must be screened to establish, not only his contemporaneous use of Vioxx at the time of the thrombotic event, but the medical factors that may confound establishing a causal connection between the thrombotic event and the Vioxx use. The paralegal will need to establish the claimant's medical history, family history, risk factors, Vioxx consumption, his baseline activity and employment status, then his injury and subsequent medical course<sup>viii</sup>.

Additionally, the person, either the Vioxx user or his representative, with whom the law office will work and whom the jury will see, needs to be assessed for stamina and personality befitting a credible plaintiff.

At about this point in data collection, the law office often does a review of the potential claimant's data and makes a decision as to whether additional investigation is warranted. Common factors that may exclude a client from further investigation beyond the initial intake include:

- The injury claimed is a hemorrhagic, not thrombotic stroke;
- There is no objective proof of Vioxx use temporally related to the injury;
- The patient has too many comorbidities, or serious illness that would confound establishing a causal connection between the Vioxx use and the injury alleged;
- The patient has no objective evidence of injury;
- The patient has a serious disease process, like cancer that will result in a shortened life expectancy or serious morbidity that will confound or dwarf the Vioxx injury;

- There are personality issues unbecoming a plaintiff;
- There is inadequate or untimely medical documentation to support the case;
- Medical records are chock full of evidence of noncompliance and/or self destructive behaviors, such as drug or alcohol abuse or self neglect; and
- The client is unable or unwilling to cooperate with the needs of the law office to develop a case.

If the Vioxx user conforms to the inclusion and exclusion criterion as defined by each law firm, then the data collection can proceed to identify the claimant's providers, past and present. Only then can the daunting task begin, in collecting the medical records, pharmacy print-outs, itemized statements, lien information, and other documents that will illustrate the elements of the Vioxx case.

Each case analysis starts with the tedious process of organizing the records and numbering and tabbing them, a job either performed by or orchestrated by the paralegal. Many "paperless" offices then scan the organized hard copies, and all subsequent reviewers then work off the electronic form of the documents.

### **Risk Factor Identification**

Because many patients who suffer injuries from Vioxx are at risk for suffering a stroke or myocardial infarction even without Vioxx, developing a causal connection between Vioxx use and the event poses a challenge. Merck will argue that patients with multiple risk factors had the thrombotic event due to factors other than Vioxx; plaintiffs will

respond that patients with risk factors should not even have been given Vioxx because the drug's effects doubled their already elevated risk of suffering a thrombotic event<sup>ix</sup>. The reality of the case often boils down to a battle of the experts.

To expedite experts' reviews of the cases to make an assessment of the causal connection, each claimant's risk factors and confounding disease processes needs to be identified. Baseline demographic information must be compiled for each potential claimant including: age, sex, ethnicity, medical history, in addition to listing his risk factors. Specific information regarding the claimant's cardiovascular status should detail his past cardiovascular medical history, co-morbidities and adequacy of his medical management, laboratory data and radiologic data reflecting cardiovascular disease status, family history, his social history, and finally, his medication history in general.

### **Documenting the History of Vioxx Use**

Data that needs to be collected relative to Vioxx use will be used to prove that Vioxx ingestion was temporally associated with the injury. In the best case scenario, appropriate, objective evidence of Vioxx use may consist of a physician's order stating the prescribed dose and frequency for Vioxx use, plus a pharmacy printout showing that the prescription was filled and refilled surrounding the period in which the user suffered his thrombotic event. A surprising number of patients save empty or partially empty prescription bottles of Vioxx, and these should be collected and marked as exhibits of which the defense is made aware, and then kept within a safe chain of custody until trial.

More often than not, the claimant's Vioxx history is not so simple to illustrate. The patient may have taken varying doses over time, stopping and starting, using different pharmacies, sharing prescriptions with other family members, etc. The goal in obtaining a Vioxx history is to document:

- Whether the person has taken Vioxx within four days (or whatever number of days the law office has deemed appropriate) immediately preceding the thrombotic event;
- The start and stop dates of each episode of Vioxx usage;
- The dosage prescribed;
- The dose taken;
- The total length of time Vioxx was used;
- Evidence of compliance with the prescribed regimen;
- Concurrent medications used, particularly drugs that effect clotting, such as nonsteroidal anti-inflammatory drugs, steroids, and other Cox-2 inhibiting drugs<sup>x</sup>, e.g., Celebrex (*generic name: celecoxib*) and Bextra (*generic name: valdecoxib*).
  - *The recent Canadian study did not provide conclusive evidence of an increased risk of MI for celecoxib, but it may be related to the low doses being consumed by the study sample, since Celebrex is also a Cox-2 drug.*<sup>xi</sup>

The supporting documents which commonly illustrate the Vioxx use include the pharmacy printouts, physician's order sheets, prescription labels, billing statements, insurance documents, and physician and nursing notes<sup>xii</sup>.

## **Timelines**

The style in which a timeline is developed can be idiosyncratic to the paralegal and/or the law office, however the information collected should document the following:

- Claimant's baseline status (independence in activities of daily living, health, employment, social status);
- Medication history, particularly evidence of the use of Vioxx in relation to the thrombotic event, allegedly caused by the Vioxx use;
- All medical attention, interventions, and diagnostics;
- The details of his thrombotic event, including objective evidence of the event and resulting injuries, the results of all diagnostics performed, which document the injury;
- His status following the injury (independence in activities of daily living, health, employment, social status);
- Evidence, if documented, of a causal connection to Vioxx use;
- Prognosis related to the Vioxx injury and to other co-morbidities, (e.g., the patient may have suffered a small myocardial infarction that may not change his life expectancy, but has a life expectancy of five years due to a concurrent cancer).

Because the timeline is developed to facilitate access to information within the medical records, it should do just that by citing the date, information source, person who documented the fact and specific page number/Bates stamp number, from which the fact was excerpted. The information cited should be accurate reflections of the medical

records; therefore direct quotes from the records are more likely, than paraphrased summaries, to depict the content accurately.

### **Documenting the Injury**

In the early stages of client intake for Vioxx litigation, many different injuries were accepted, because the effects of Vioxx on a large human population were yet to be seen. Our working knowledge about Vioxx injuries is still being developed as clinicians compare notes about what happened to their patients and as researchers re-examine data collected in medical studies. Currently, objectively provable myocardial infarctions and strokes are the only injuries that most law offices accept as being clearly causally related. Other injuries in the grey zone might include pulmonary emboli; arterial clots that lodged in extremities or in the arteries leading to the kidney (renal emboli) or leading to the gut (mesenteric emboli), and deep vein thromboses (DVT's).

Events that are not usually accepted as injuries for purposes of litigation, include hemorrhagic strokes, edema or fluid retention, hypertension, liver and kidney problems, gastrointestinal problems, and events in which there are no objective signs of injury to explain the patient's signs and symptoms, e.g., cardiac ischemic events, (new onset angina or changing angina), and/or transient cerebrovascular events [transient ischemic attacks (TIAs) or RINDs (Reversible Ischemic Neurologic Deficits)].

The paralegal will search the medical documents, for objective evidence supporting the injury claimed. To be able to find the meaningful documents, the paralegal needs to

armed with a list of studies and physical findings that are considered appropriate evidence of injury. For example, if the alleged injury is a pulmonary emboli, the paralegal will include in the timeline, results from diagnostic studies: arterial blood gas measurements from the time of the event, CT scan results, D-Dimer results (a blood study that demonstrates that a significant amount of clotting has occurred) and physical findings, on which the clinicians relied to make the diagnosis. In the event the injury is a myocardial infarction, critical evidence may lie in electrocardiogram reports; laboratory results such as cardiac markers (e.g., troponins and CPK MBs); echocardiograms and other studies reflecting the wall motion of the heart; ejection fractions; vital signs, cardiac outputs, etc. If the injury is a stroke, the paralegal would seek documentation of neurological deficits documented in reports of examinations, as would be detailed in neurological consultations or progress notes; evidence of brain injury on MRIs or CT scans of the head, etc. that are consistent with thrombotic or embolic strokes, *not* hemorrhagic strokes.

Potential claimants who did not seek treatment at the time of the event, so that their injuries were not diagnosed and documented in a timely manner, will probably be screened and included in the initial client group, but should know that without good evidence of injury and causation, they may be excluded later.

## **CONCLUSION**

Though the expert will ultimately make the determination as to whether the injury is causally connected to Vioxx use, the litigation team must have an adequate knowledge base to sift through the clients' case presentations and determine which clients warrant the time and expense of additional investigation. Generally, the paralegal is the key team member in data collection, so his understanding of the involved pathophysiology is crucial for information gathering to allow the litigation team to make good client selections. With more than 80 million people using Vioxx between 1999 through 2004 suffering countless injuries, Vioxx litigation is certain to continue for years. Paralegals involved in medical cases should take every opportunity to familiarize themselves with these issues, because a Vioxx case is sure to come across your desk one day soon.

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<sup>i</sup> Mukherjee, D., Nissen, S.E. Topol, E.J. (2001, Aug 22-29) Risk of cardiovascular events associated with selective COX-2 inhibitors. JAMA, 954-9.

<sup>ii</sup> <http://www.npr.org/templates/story/story.php?storyId=5400413>

<sup>iii</sup> Bresalier, R.S., et al. (2004). Cardiovascular events associated with rofecoxib in a colorectal adenoma chemoprevention trial. New England Journal of Medicine. 352 (11). 1092-1102.

<http://content.nejm.org/cgi/content/abstract/352/11/1092>

<sup>iv</sup> Levesque, LE, et al. (2006). Time variations in the risk of myocardial infarction among elderly users of COX-2 inhibitors. Canadian Medical Association Journal. 174, (11).

<sup>v</sup> <http://www.npr.org/templates/story/story.php?storyId=5400413>

<sup>vi</sup> Pritts, D. (2006). Vioxx® . . . more to the story. Journal of Legal Nurse Consulting, 17, (2). 11-15.

<sup>vii</sup> <http://www.htwlaw.us/>

<sup>viii</sup> Donati, M. (2005). Defending a Giant. LiNC. 13, (2). 3, 9-10

<sup>ix</sup> FitzGerald, G. & Patrono, C. (2001). The coxibs, selective inhibitors of Cyclooxygenase-2. New England Journal of Medicine, 345, 433-442.

<sup>x</sup> Donati, M. (2006). Defending a Giant: Vioxx®. Journal of Legal Nurse Consulting, 17, (2). 16-17.

<sup>xi</sup> Levesque, et al, online pg 6.

<sup>xii</sup> Donati, (2006), 17.