# Focusing on Basics, Including Drug-Use Policy, Remains Important for Today's P&T Committee

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## Introduction

In a 2004 issue of *P&T*, Balu et al. reviewed the changing role of the P&T committee:

> [P&T] committees evaluate the clinical use of medications and develop policies for managing access to them and for ensuring effective drug use and administration. … From the focus on rational medication choices to the practice of monitoring adverse drug reactions and operating within an organization's budgetary limits, the duties of P&T committees have been continuously expanding and evolving.[1,2]

While that remains a bedrock summary of key P&T work, significant changes were under way by the end of 2014. P&T committees were evolving to deal with care at expanding sites within an organization, across a larger system, or involving multiple organizations. At that time, Vogenberg and Gomes[3] described market and regulatory changes that were causing care delivery models to evolve, merge, or change from their origins. Still, throughout the years and alterations in scope, the core function of the P&T committee has not necessarily changed. In fact, as the authors pointed out in 2014, the importance of P&T committees may have grown.

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The Joint Commission, the American Medical Association, and all of pharmacy's professional societies have promoted sound drug formulary systems, solid medication use policies, and best practices for hospital and health-system pharmacies. Beyond licensing pharmacists, the pharmacy profession, like many others, establishes standards of practice in accordance with federal and state law. Such standards find their way into policies and procedures used by health care delivery organizations, such as hospitals, health systems, clinics, and pharmacies, where and/or when medications are involved in clinical practice.

## Duties and Responsibilities

Within hospitals and health systems as a result, the P&T committee is important as a group responsible for overseeing all aspects of drug therapy in an institution.[4]

The Joint Commission establishes medication management standards that are continuously reviewed, updated, and used in surveys of accredited organizations. These standards include developing policies and procedures around medication management, use, dispensing, monitoring, evaluating, responding to potential adverse events and medication errors, and assessing medication management systems for risk to patients in order to improve safety, among other elements.[5]

A variety of system failures can relate to medication use, some as simple as a pharmacy technician signing an order form as a pharmacist to procure drugs. In a closed case, *Banks v Regions Hospital*, the technician filled out an order form to initiate a free trial program with a pharmaceutical manufacturer so the hospital would receive drugs for its patients. A court found that this constituted employment misconduct. However, whether a pharmacist's signature is necessary for product acquisition can be debated. The permitted role of a technician or a pharmacist can be based on hospital policy rather than laws or rules, according to the court. So in the supply chain to, from, or within the hospital, pharmacy department policies in accordance with P&T committee and executive medical staff policies need to be monitored.[6]

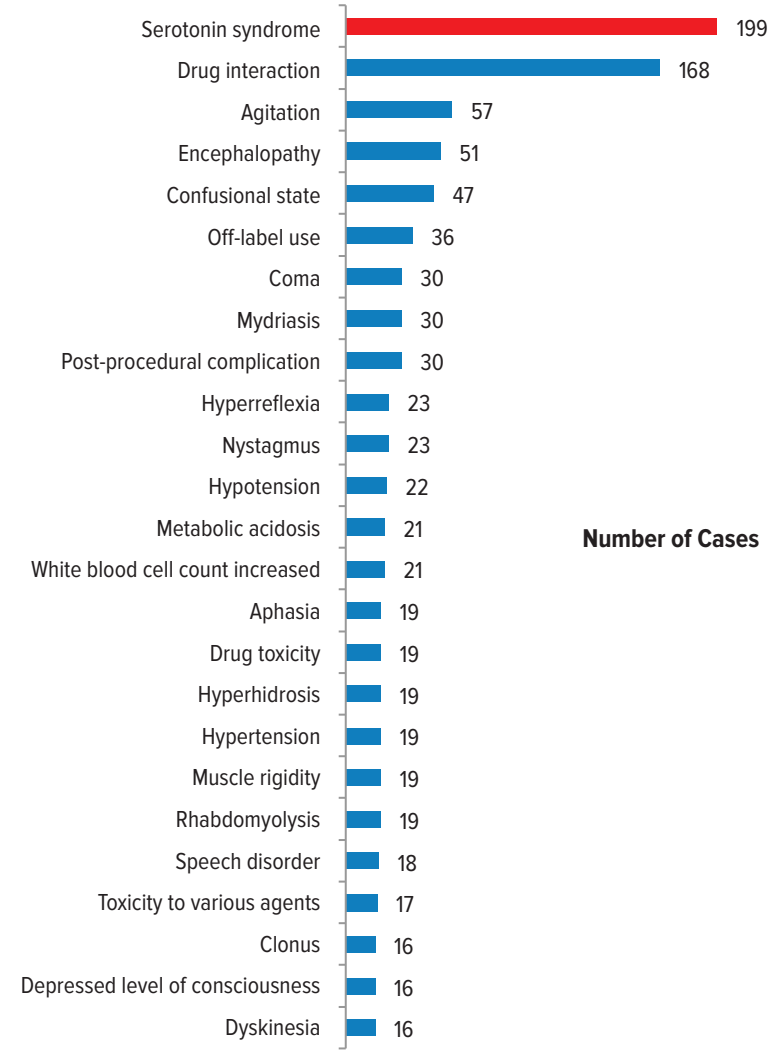
## An Illustrative Case Of Systems Failure

One example of a multiple-systems failure centered on medication reconciliation that helped result in a brain-damaged patient and a $20.5 million verdict against a drug manufacturer.[7] The facts in what started as a case against the surgeon, pharmacist, and hospital ultimately led to a verdict against the drug manufacturer—a stroke of some luck for the other parties.

The case involved a middle-aged woman who was screened and preadmitted for thyroidectomy surgery. As part of the preadmission process, methylene blue dye was ordered to help the surgeon visualize the thyroid and parathyroid gland structures—a common use of the dye.[8] The patient's home medication history included venlafaxine (Effexor, Pfizer). The hospital pharmacy prepared an intravenous (IV) methylene blue infusion (500 mg in 500 mL normal saline), which was administered one hour before surgery. Following surgery, the patient did not wake up; she experienced blood pressure swings and clonic seizures. Subsequently, she was admitted to the intensive care unit with a diagnosis of serotonin syndrome, most likely caused by the interaction of methylene blue and venlafaxine. Coma was induced and maintained for three weeks. The comatose patient was transferred to a university hospital, where she recovered with significant neurological deficits. She returned to work three months later at a much lower cognitive function and retired early due to cognitive problems. The patient sued the surgeon and the hospital for administering the dangerous combination of methylene blue and venlafaxine.

Medication reconciliation had been performed upon admission, but the pharmacist testified that the hospital's pharmacists did not usually consider home

**Figure 1 Most Frequently Reported Reactions With Methylene Blue***




* Based on FDAble search on November 22, 2016.[10]

medications, nor did the hospital and pharmacy software screen home medications against new medication orders, so this was not done automatically. The pharmacist testified that methylene blue orders were received a few times a year using a preprinted order set. The pharmacist also testified that because she was not familiar with methylene blue, she checked the package insert and found no warnings about interactions between venlafaxine and the dye. She did not, however, check the venlafaxine package insert (which contraindicates the methylene blue combination), nor did she check any external drug interaction software—such as Drugs.com, which clearly identifies the combination interaction risk as "major" (in red text) and indicates that coadministration is contraindicated.[9]

As part of experts' case review, a search and analysis of the Food and Drug Administration (FDA) MedWatch database was conducted by FDAble in November 2016 for methylene blue, interaction medications, and adverse events.[10] Serotonin syndrome is the most commonly reported adverse reaction when methylene blue is reported as a suspect or interacting medication in an adverse event case (Figure 1). Specifically, 43.7% of cases (199 of 455) that reported methylene blue also reported serotonin syndrome. A search of "serotonin syndrome," "methylene blue," and "serotonin modulators" found:[10]

- Almost all of the 199 cases (97%) also co-reported administration of a serotonin-modulating medication
- Serious outcomes of these cases (methylene blue plus a serotonin modulator) included 10 deaths and 142 hospitalizations (Figure 2)

Subsequently restricting the search to adverse event cases where methylene blue was co-reported with venlafaxine resulted in the following findings:[10]

- Serotonin syndrome was the most commonly reported adverse reaction when venlafaxine was co-reported with methylene blue in an adverse event case. A majority of venlafaxine/methylene blue adverse event cases also reported serotonin syndrome (17 of 33 cases)
- Serious outcomes included nine deaths and 18 hospitalizations (Figure 3)

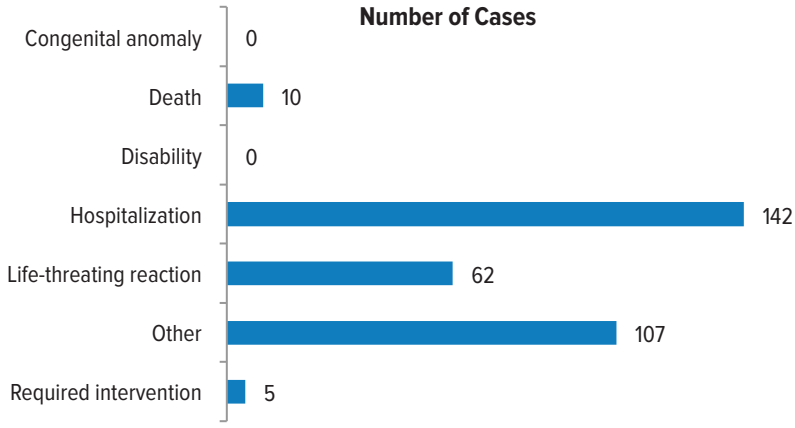
Critical performance issues for the pharmacist and the hospital in this case, identified by pharmacology and pharmacy experts, included the following:

- Failure to detect and warn about the interaction between venlafaxine and methylene blue
- Failing to have a computer system or other reliable functioning system in place to screen the September 10, 2013, order for methylene blue for the patient against her known home medications, including venlafaxine, for potential harmful interactions
- Failure to have policies and procedures in place directing pharmacists and assistants to confirm that the order for methylene blue was screened against her known home medications, including venlafaxine, for potential harmful interactions

In court, both the patient's surgeon and the anesthesiologist testified that they relied on the pharmacist to screen for drug interactions. The hospital's policy and procedure described a screening duty, as does the American Society of Health-System Pharmacists' Practice Guidelines.[11]

The pharmacist also agreed that there was a duty to screen—but she blamed the oversight (and thus the life-threatening

**Figure 2 Patient Outcomes: Methylene Blue[a] Plus Any Serotonin Modulator[b]***

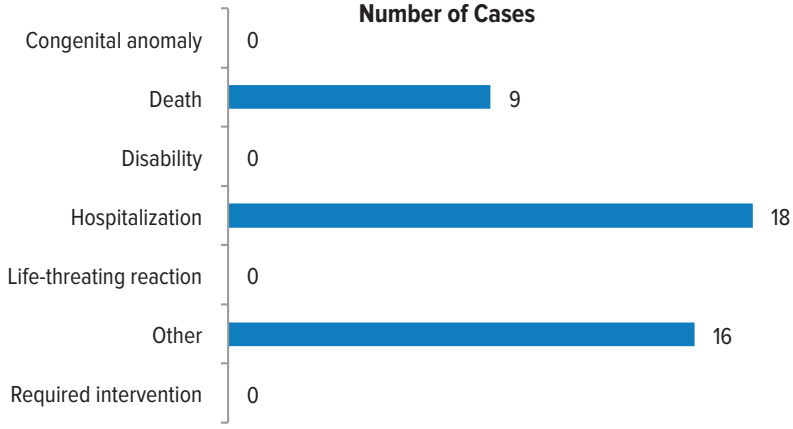



* Based on FDAble search on November 22, 2016.[10]

[a] Includes any of the following synonyms: methylene blue, basic blue, calcozine blue, ceruleum methylenum, chromosmon, methylenblau, methylenium ceruleum, sandocryl blue, solvent blue 8, urolene blue.

[b] Includes: carbamazepine, citalopram, clomipramine, duloxetine hydrochloride, Effexor, escitalopram, fluoxetine, fluvoxamine, Kytril, lamotrigine, mirtazapine, palonosetron, paroxetine, Paxil, pexeva, Prozac, quetiapine, seralin, Seroquel, sertraline, SRI (unspecified), SSRI (unspecified), tramadol, trazodone, venlafaxine.

**Figure 3 Patient Outcomes: Methylene Blue[a] Plus Venlafaxine[b]***




* Based on FDAble search on November 22, 2016.[10]

[a] Includes any of the following synonyms: methylene blue, basic blue, calcozine blue, ceruleum methylenum, chromosmon, methylenblau, methylenium ceruleum, sandocryl blue, solvent blue 8, urolene blue.

interaction) on the absence of the warning in the methylene blue package insert. Based on this testimony, attorneys for the injured patient sued Akorn, the manufacturer of the methylene blue injection that was used in the case. Akorn admitted knowledge of the interaction, but claimed that since methylene blue was a grandfathered drug and not the subject of a "new drug application," Akorn was not able to include the interaction warning about serotonin syndrome with selective serotonin reuptake inhibitors. A different manufacturer of methylene blue, American Regent, *did* provide the warning in its package insert for the product, even before it was awarded an NDA for methylene blue.

The hospital, its pharmacy, the pharmacist, and the surgeon were dismissed from the case before the trial, which was conducted with Akorn as the only defendant. Akorn maintained its position that it could not warn and blamed the pharmacist for not warning the surgeon and avoiding the drug interaction injury. An FDA labeling expert testified that Akorn had a duty to include the warning and could have done so. A jury found Akorn liable and negligent, considered its behavior egregious for not providing a warning of the drug-interaction risk, and awarded compensatory and punitive damages to the injured patient totaling $20.5 million.[7]

After the incident, the hospital pharmacy learned that its software had a feature to screen home medications with active orders—but that feature had not been activated. Following the injury, home medication screening was added to the software-driven drug-interaction screening.

## P&T and Administrative Concerns and Issues

The outcome in this type of case has many implications, including, for starters, institutional and multidisciplinary practice, P&T committee responsibilities, and reliance on manufacturers' package inserts. While the jury attributed no fault to the pharmacist or the surgeon in the post-verdict jury poll, the result could have been very different if the correctly labeled American Regent product had been used.

Had the case unfolded in a different way, the P&T committee could not have escaped responsibility on behalf of its organization for a system failure such as the one described. In addition, this case could have triggered a continuous survey by The Joint Commission, exposing the organization and its employees to loss of accreditation.

Professionally, such a case contains many moral and ethical issues for today's larger, more complex organizations. For example, is it an employed person's responsibility as a health care professional to take on what could be perceived as an unnecessary action based on the starting facts of the case? Can a health care professional rely on his or her organizational structure to provide a level of due diligence that addresses core patient care values at the level of any individual case? What standard of care can a patient

expect in an accredited organization on any given day, time, or circumstance? What professional duty does a physician or pharmacist have to themselves, to their co-workers, and to patients on each encounter or care activity?

## Summary and Recommendations

The P&T committee has a long history of purpose, status, and responsibility within health care organizations that continues today. The question becomes: How does such a committee work within the modern health care delivery organization? How does the P&T committee ensure that its core duties are executed throughout the organization and that other committees interact with it or support it in the now-more-complex execution of its responsibilities?

Based on the evolution of health care delivery to date and its likely state two or three years from now, it appears incumbent on organizations to reflect upon their operational performance to determine how best to sustain such core entities as the P&T committee. Identifying the support and resources needed for P&T committees to meet their responsibilities in the modern health care organization seems to be a logical starting point before risk management takes over in an ever-more-litigious environment. In advance of such defensive positions and a potential downward spiral in patient treatment, care delivery organizations have a chance to address the situation with positive steps.

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