Upcoming Book: Ira P. Gunn
To the editor: At the upcoming Annual Congress in Salt Lake City the AANA will release the newly published book Ira P. Gunn, Nurse Anesthetist.

For my co-editors and me, work on the book was a true labor of love and an exploration of the genius Ira was. We each knew Ira in different ways and at somewhat different times, but we each learned from and sought to incorporate her essence in our lives and in this book.

Within the pages we have endeavored to bring that essence and brilliance to you; Ira’s progenies and legacies. Ira worked tirelessly to advance the profession of nurse anesthesia and nursing as a whole as a clinician, educator, consultant and unyielding advocate, as both a member of the military and as a civilian. Her thoughts and writings were so prescient that many of her ideas are still as valid today as when she wrote them decades ago.

Some of her work is scholarly, some personal. It is always thoughtful and circumspect, often feisty. Yet the thread of caring for her fellow humans and particularly her colleagues, students and profession is evident throughout.

Through her book chapters, journal articles, OpEds, letters to the editor, emails and even her voice at the microphone at so many AANA business meetings, it is our hope that each of you—her colleagues, friends, students and particularly the students of the future—can gain a better understanding of the history, present and future of the profession and world Ira loved and irrevocably changed.

Please stop by the AANA PR booth in the exhibit hall to order your copy, share memories of Ira, and learn more about this icon of the profession.

Jay Horowitz, CRNA, BSN, ARNP
Maura McAuliffe, CRNA, PhD, FAAN
Rita Rupp, MA

Shake Up in the Neostigmine Methylsulfate Cholinesterase Inhibitor Market for Neuromuscular Block Reversal
To the editor: It appears that the days of inexpensive NMB reversal by cholinesterase inhibitors, particularly neostigmine, are coming to an end. Neostigmine at a few dollars a vial has been the benefit of non-brand manufacturers who support our markets. Regulatory enforcement and business maneuvering may end this one economic benefit of neostigmine by removing some manufacturers and increasing the price. Two pharmaceutical companies, Éclat Pharmaceuticals (702 Spirit 40 Park Drive, Suite 108. Chesterfield, MO 63005) and Fresenius Kabi (Grand Island, NY) have received FDA approval for branded neostigmine methylsulfate injections.1,2 Bloxiverz (neostigmine methylsulfate) manufactured by Éclat Pharmaceuticals which was FDA approved May 31, 2013 has recently undergone a price increase to $98.75 per vial.3 The 10 mL multi-dose vials are in two strengths (0.5 mg/mL and 1 mg/mL).4 Neostigmine for years has been priced well below $10.00/vial.

Brand drugs historically cost more than non-branded but brand drugs usually come down in price by competition once generic manufacturers enter the market. The US competing market forces in the case of neostigmine may be removed by FDA enforcement action spurred by pharmaceutical industry interest. Petition by Éclat Pharmaceuticals to the FDA has requested “expedited enforcement action requiring that these manufacturers immediately remove the unapproved injectable neostigmine methylsulfate products from the market because they are competing with an FDA-approved drug product (NDA 204078, Bloxiverz neostigmine methylsulfate injection”).5 Generic drugs must be FDA approved, as are brand drugs, but some manufacturers have produced and sold neostigmine without required approval. The FDA Marketed Unapproved Drugs—Compliance Policy Guide (CPG), outlines the FDA regulatory intention to remove these drugs from the nation’s supply.6 The petition by Bloxiverz manufacturer Éclat Pharmaceuticals specifically lists the following as companies that market non-FDA approved neostigmine: “Cardinal Health (1 mg/mL) West-Ward Pharmaceuticals Corp. (0.5 mg/mL and 1 mg/mL) Fresenius Kabi USA, LLC (0.5 mg/mL and 1 mg/mL) American Regent, Inc. (0.5 mg/mL and 1 mg/mL) General Injectables & Vaccines, Inc. (1 mg/mL)” 5p1

The rationale for this removal of non-FDA approved drugs is safety but less competition also allows for price increases as clearly dis-
closed by the recent price increase of neostigmine methylsulfate brand Bloxiverz to $98.75 a vial. Market analysis has found neostigmine prior to Bloxiverz: “vials sold for approximately $4-5 and the $20 million market consisted of Westward Pharmaceuticals, American Regent (which voluntarily left the market in November 2013) and Fresenius. Westward and American Regent each had approximately 40-50% of the market and Fresenius was a relatively minor player at 10-15%.”

It remains to be seen if or when these makers of neostigmine are removed from marketing neostigmine. It further remains to be seen if any remaining manufactures will be able to fill the void of demand. Considering the FDA’s positive actions to improve generic propofol availability over the past several years to alleviate shortages, it would be strange that this same agency would create a shortage or undue burden on anesthesia providers.

A caveat mentioned in the FDA’s CPG states: “FDA intends to evaluate on a case-by-case basis whether justification exists to exercise enforcement discretion to allow continued marketing for some period of time after FDA determines that a product is being marketed illegally. In deciding whether to allow such a grace period, we may consider the following factors: (1) the effects on the public health of proceeding immediately to remove the illegal products from the market (including whether the product is medically necessary and, if so, the ability of legally marketed products to meet the needs of patients taking the drug); (2) the difficulty associated with conducting any required studies, preparing and submitting applications, and obtaining approval of an application; (3) the burden on affected parties of immediately removing the products from the market; (4) the Agency’s available enforcement resources; and (5) any special circumstances relevant to the particular case under consideration. However, as stated above, FDA does not intend to apply any such grace period to an unapproved drug that was introduced onto the market after September 19, 2011.”

Free markets and competition often have a way of settling imbalances and the FDA’s approval of another branded neostigmine methylsulfate manufactured by Fresnius Kabi may bring price stability. In the meanwhile we may want to prepare for the possibility that inexpensive NMB reversal may become a thing of the past. If neostigmine reversal stays close to $95.00 a vial we in the pharmacy and anesthesia departments will need to adjust accordingly. How that is done remains to be determined. Will we use neuromuscular blocking agents less? Will we switch to other cholinesterase inhibitors for neuromuscular block reversal (edrophonium, pyridostigmine)? Will sugammadex, with FDA approval, become the better option considering the new price comparisons and its greater efficacy? These questions have yet to be answered and new questions will likely emerge as we move forward in this developing era of pharmaceutical advancements in efficacy and price. The American Association of Nurse Anesthetists (AANA) is in communication with the FDA to address these issues and serve the nation’s patients and CRNAs for continued access to necessary resources.

Table. Commonly Used Anticholinesterases, Anticholinergics, and Selective Relaxant Binding Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose range (µg/kg)</th>
<th>Onset (min)</th>
<th>Duration (min)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neostigmine</td>
<td>25-75</td>
<td>5-15</td>
<td>45-90</td>
<td>Most commonly used reversal agent; may increase incidence of postoperative nausea and vomiting.</td>
</tr>
<tr>
<td>Pyridostigmine</td>
<td>100-300</td>
<td>10-20</td>
<td>60-120</td>
<td>Slow onset, long duration, and slow reversal. Rarely used.</td>
</tr>
<tr>
<td>Edrophonium</td>
<td>500-1000</td>
<td>5-10</td>
<td>30-60</td>
<td>Not recommended for deep block; rapid onset, short duration.</td>
</tr>
<tr>
<td>Atropine</td>
<td>15</td>
<td>1-2</td>
<td>1-2hr</td>
<td>Should not be combined with edrophonium because of more rapid onset.</td>
</tr>
<tr>
<td>Glycopyrrolate</td>
<td>10-20</td>
<td>2</td>
<td>2-4 hr</td>
<td>Less initial tachycardia than atropine; no central nervous system effects; most frequently used.</td>
</tr>
<tr>
<td>Sugammadex</td>
<td>2-16</td>
<td>1-2</td>
<td>2-16 hr</td>
<td>Selective relaxant binding agent; up to 16 mg/kg has been safely used.</td>
</tr>
</tbody>
</table>

REFERENCES
6. Guidance for FDA Staff and Industry. Sec. 440.100. Marketed New Drugs Without Approved NDAs or ANDAs Marketed Unapproved Drugs—Compliance Policy.
...to the bottom of the deep blue CPC...

To the editor: The Continued Professional Certification (CPC) program of the National Board of Certification and Recertification for Nurse Anesthetists (NBCRNA) remains controversial.1,2

Regardless of one’s view, the CPC program harbors unintended consequences, remains poorly accepted by CRNAs, and has the potential to exert a devastating impact on AANA membership.

No consolation should be taken from any attempt to minimize the importance of the CPC Examination (CPCE) (eg, claiming the CPCE will be “manageable”). False reassurance rings empty and threatens the very integrity of the CPCE by minimizing its rigor. Neither should any consolation be given by suggesting that the CPC will come into full blossom 17 years from now. Kicking the current CPC problem into the laps of our current younger AANA members is simply unacceptable.

The CPC is complicated. Core Modules (CM) are linked to the high-stakes CPCE via the CM objectives. Excess CM credits may substitute for required Class A credits; excess Class A credits will count towards Class B requirements. Class A credits require testing; Class B do not. How validate Class B activities? The overlapping of categories argues for simplification. Why define distinctions that lack actual differences?

Core Modules predictably will consume the limited resources of CRNAs who will focus on them to help “pass the test”. Thus the CM will exert paradoxical and perverse effects of 1) inhibiting CRNAs’ participation in expert level educational activities, and 2) discouraging attendance at Class A Continuing Education (CE) offerings at local, state, and national, and international venues. The NBCRNA has imposed requirements on CM vendors that are stiflingly burdensome, and that insulate NBCRNA from the costs and risks which vendors must assume in toto.

The voluminous entry-level objectives of the CM are linked to the CPCE. How the CPCE will measure “expert knowledge and clinical judgment” remains unclear. Failure to pass the CPCE will result in a loss of recertification as a nurse anesthetist, loss of licensure in some states, loss of insurance reimbursement, and a loss of the ability to practice in the specialty.

With the CPCE, the NBCRNA sets the bar astonishingly high for CRNAs. Physicians opt for certification, and they may continue specialty practice regardless of recertification status without threat to licensure. Where is the evidence linking recertification (or certification) of nurse anesthetists to quality of care? While studies addressing initial certification or licensure or the feelings of trainees may be cited3,4,5 to support the CPC, none of these studies address the topic of recertification. The CPC addresses recertification;
chooses. Why would it not?

In the meantime, the CPC remains a solution in search of a problem. If the problem is one of anesthesia safety, then that solution has been found among nurse anesthetists who have made the specialty safer than ever. If the problem consists of the need to match other specialties’ recertification mis-steps (Where are the lemmings? Where is the cliff?), then CRNAs will incur substantial burdens in time, expense, and distraction in conforming to requirements which among other specialties have proved problematic.

REFERENCES

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DISCLOSURES
The author has no conflict of interest or financial involvement in the subject material.

CPC: Take Care When Interpreting the Evidence
To the editor: In reviewing the June 2015 letter to the editor, “CPC: One Member’s Perspective” by Dr Frank Titch,1 I felt compelled to clarify data presented to prevent readers from drawing wrong conclusions or making inferences from incomplete or inaccurate information.

In June 2014, two independent polls were conducted of CRNAs who had attended continuing education meetings offered by two vendors.2 CRNAs in both polls responded overwhelmingly that they felt uninformed regarding the CPC and that they had not had input to the CPC development processes. The Titch letter states “4.5% of the total membership felt they did not have an opportunity to have input into the CPC program and 6.2% felt ill-informed about the CPC program.” This information is incomplete and may lead readers to draw wrong conclusions. The two polls conducted did not survey the total AANA membership at all. Rather, 2,781 and 2,230 CRNAs respectively (unknown if AANA members or not) were polled by two separate entities and both received similar results. Hence, to say that only 6.2% of the total AANA membership does not feel well informed and that only 4.5% feel they had no input to the CPC is factually inaccurate and could lead some to falsely conclude that only a small minority of AANA members share these concerns. On the other hand, if one chooses to assume that CRNAs polled may have represented the total AANA membership, as could be inferred in the Titch letter, then one could state that 88.7% (35,220) of the membership, not 6.2%, feel ill-informed and that 66.3% (26,326) of the membership, not 1.1% (432 people), supported the “no confidence” resolution. This is cause for further investigation.

Dr Titch indicated his review of “…the analysis of surveys conducted by both the AANA and the NBCRNA along with 58 references…” Several comments seem in order. In my read, I find no published survey to date of AANA members being conducted by the AANA regarding the CPC in its present or past forms. Time must be granted to allow the AANA to conduct this work. Additionally, literature cited as a rationale for the CPC is, in my read, not reflective of any measurement of the CPC or the CRNAs and patients affected by the CPC. For instance, Hawkins et al3 cited several studies which have suggested that 1) board-certified physicians provide better care than...
those without certification and 2) that physicians with higher scores on the initial board examinations provide higher quality of care than those with lower scores. Though interesting, the above findings do not serve as a rationale for the proposed CPC, which is a recertification (not initial certification) modality for CRNAs. All CRNAs are already certified.

I believe the inconclusive nature of the information presented above provides compelling evidence for the AANA to support and enhance a continued national dialogue on the CPC. I call upon the AANA to consider a thorough and independent scientific examination of the AANA membership on this matter. This will take time and cost money to be properly performed and I ask AANA members to support the Board with such an endeavor. If truly only 1.1% of the total AANA membership have no confidence in the proposed CPC as reported by Dr Titch is true, then the AANA can feel confident that it is best serving the membership and that implementation of a new CPC will be broadly embraced and members will continue to support their Association. On the other hand, if the 66.3% supermajority vote of the members present at the 2014 business meeting is representative of the broader AANA membership, then moving ahead to implement a new CPC without significant stakeholder buy-in could prove detrimental to the Association and ultimately to the public that relies upon CRNA services.

I join Dr Titch in encouraging every CRNA to thoroughly examine and properly interpret the evidence. I also call upon CRNAs to support AANA leaders in getting their own more definitive AANA data and engaging and educating stakeholders in this process.

REFERENCES

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DISCLOSURES
The author was first chair of the National Board of Certification and Recertification for Nurse Anesthetists.

With these additional letters this particular topic, CPC, is now closed and no future letters on this topic will appear. We thank the authors of all the letters sincerely for their valuable contribution to AANA Journal.

—The Editor in Chief