

# Emerging Subspecialties in Neurology: Clinical development

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Therapeutic development includes the activities necessary to bring a new medicinal compound (chemical or biologic) or medical device to market. Following drug discovery or development of a new device, successful preclinical studies result in an Investigational New Drug (IND) application (United States only; Clinical Trials Exemption Certificate in the United Kingdom). Once the IND is filed, a team-driven process begins that tests the efficacy and safety of a new therapeutic in humans. This process, known as clinical development, has traditionally been divided into 4 phases, with large-scale phase 3 pivotal trials in patients with a specific disease leading to registration and postmarketing studies.<sup>1</sup>

Recent advances in understanding the pathophysiology of neurologic diseases has led to the discovery of many new drug targets and candidate drugs. The largest funding agencies for research, represented by the NIH and the pharmaceutical industry,<sup>2</sup> have substantially increased their budget allocation to neurosciences research<sup>3</sup> and devoted more resources to clinical development programs.<sup>4</sup> Thus, there is a significant and growing need for neurologists with experience and relevant training in clinical development.

Despite the growing need and potential rewards, recognition of therapeutic development careers among neurologists is generally poor. Furthermore, neurologists not directly involved with pharmaceutical medicine often have a poor understanding of the process, in part because it is largely ignored in US medical education. Here we review clinical development and training opportunities for interested neurologists.

**Opportunities for neurologists.** Clinical development opportunities for neurologists exist at pharmaceutical and device companies, contract research organizations, academic research organizations, regulatory agencies (e.g., US Food and Drug Administration, European Medicines Agency), and as an independent contractor. Increasingly, industry has partnered with academia to reduce rising research and development costs and take advantage of cutting-edge research at academic institutions. Industry sponsors potentially

benefit from the specialized technology and expertise available in the academic environment. In this setting, academic neurologists work within their research area on innovative projects of interest to industry.

**Roles.** Clinical development activities of neurologists usually take advantage of their medical training and clinical experience. For example, in the early stages of a novel therapeutic's clinical development, neurologists must understand and communicate the potential clinical benefits of the new agent, disease populations to evaluate in clinical studies, and perceived safety risks that require monitoring.

To evaluate the desired clinical benefits and minimize safety risks to research volunteers and patients, clinical development neurologists often offer their skills in multiple roles. These include activities such as developing clinical trial medical monitoring, and safety signal detection protocols; assisting with development of clinical trial reports, regulatory documents, and investigator brochures; directly monitoring the safety of trial participants; ensuring the medical accuracy of printed materials, such as product labels and publications; answering medical questions from investigators; and providing therapeutic training for internal staff, investigators, and contractors.

**Functions.** Neurologists can contribute to clinical development in several capacities; notably, as site investigator, clinical research physician on a clinical development team, or an external consultant. Neurologists with appropriate training may also support clinical development as a clinical pharmacologist.

**Neurologists in industry.** Within a pharmaceutical/device company or contract research organization, neurologists usually provide services as a medical affairs, clinical research, or safety physician. Due to the complexities of the therapeutic development process, neurologists often work in multidisciplinary teams with representatives from multiple functions (e.g., clinical operations, regulatory affairs, statistics). Importantly, the contributions of the neurologist will be interpreted in the context of input from these other functions that also play critical roles.

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**Pathways for entering industry.** Neurologists may enter clinical development in an academic or industry environment directly after completing their clinical training. Most commonly, neurologists participate in clinical development as an investigator in pharmaceutical industry–sponsored clinical trials. Typically, their role starts as a subinvestigator in a clinical trial during training or as junior faculty, leading to a principal investigator role with increasing experience and participation in a variety of trials. Neurologists perceived as experts in their respective fields also sit on advisory boards to provide scientific advice on concepts and the development of clinical trial protocols. In some trials, external physicians serve on data monitoring committees that evaluate safety or efficacy data. After participating in clinical trials as an investigator or advisory board member, neurologists may decide to pursue clinical development as a career in the pharmaceutical industry.

**Similarities and differences among clinical medicine, academic research, and clinical development.** In contrast to clinical practice, where neurologists try to achieve a clinically meaningful change in disease status in the individual patient, clinical development of a therapeutic entity emphasizes the population response. In the industry setting, many team members share decision-making responsibilities and regulatory agencies (and increasingly payers) strongly direct clinical development activities. In translational or basic academic research, decisions are more centralized and often based on personal interests, skill sets, and funding opportunities. Clinical practice decisions may also be influenced differently by payers, legislation, and legal considerations. Additional challenges for a career in the pharmaceutical industry may include differences in terminology, organizational structure, and the highly regulated environment. Although seemingly straightforward, the distinctions between these environments and the necessary change in mindset can be difficult for neurologists who enter clinical development from a prolonged period in clinical practice or academic research. Despite these differences, communication, teamwork, and a strong desire to improve patient health are common elements in all these settings, while adherence to good clinical practice guidelines should be a feature of all clinical research.

For many neurologists, clinical development is a nontraditional career path. However, they may be attracted to the challenging work on the cutting edge of therapeutics, access to innovative technologies, and involvement in rapidly advancing clinical research without the stress of maintaining grant funding. Additional potential attractions include the often-employed multidisciplinary team approach and collaboration; a sense of accomplishment when a new medicine is delivered to the market for patients

with unmet medical needs or a study is successfully completed; varied daily activities; and the need, during the development lifecycle of a therapeutic entity, to overcome ever-changing challenges. Neurologists may be enticed by the change in responsibilities, perceived lifestyle benefits, prior positive experiences interacting with industry personnel, and the global scope of clinical development.

**Training opportunities.** In several countries, pharmaceutical medicine is a recognized medical specialty with dedicated training programs and licensing.<sup>5</sup> For instance, in the United Kingdom, the Pharmaceutical Medicine Specialty Training program is a multiyear modular training program, including a module on clinical development, that leads to registration with the General Medical Council as a specialist in pharmaceutical medicine.<sup>6</sup> Particularly in Europe, advanced training opportunities in pharmaceutical medicine often confer a master's degree.<sup>5,7</sup> Given the global nature of the pharmaceutical industry, the International Federation of Associations of Pharmaceutical Physicians harmonized these training programs to provide a balanced education and professional degrees that are recognized between countries. These structured pathways do not exist in the United States and training is often individualized to the needs of the neurologist and his or her organization.

When initiating a clinical development career in industry, the highly regulated environment and inadequate exposure of many neurologists results in a protracted “startup time” with substantial training costs to their organization and lower productivity that can be reduced by prior training. Consequently, for clinical development positions, neurologists with prior training or experience will be particularly attractive.

Several opportunities exist to develop skills in therapeutic development, either in preparation for a full-time position or to improve understanding and performance in clinical trials as an investigator (table). Several organizations provide short courses, Webinars, and online courses to acquire knowledge in specific areas of clinical development, as well as longer, usually site-based courses that offer a broad overview of the therapeutic development process.

Neurology-specific structured training opportunities, such as fellowships, are limited. We know of 3 intensive programs that focus on drug development training in the neurosciences (UCB Pharma, Inc., in partnership with the University of North Carolina Eshelman School of Pharmacy, Duke Clinical Research Institute, and Hamner Institutes; University of California, San Diego; and University of Rochester).<sup>8–10</sup> Further information on these programs is available on their respective Web sites (table).

Collectively, these programs train future leaders in neurology clinical development. In addition to the

**Table** Summary of available general and neurology-specific drug development educational programs

Program	Comments
<b>Drug development fellowships</b>	
<b>PhRMA Foundation Fellowships</b>	<ul style="list-style-type: none"> <li>• Duration: 2 years; US citizens or permanent residents only</li> <li>• Clinical pharmacology focused</li> <li>• Separate medical student and faculty development awards</li> <li>• <a href="http://www.phrmafoundation.org">http://www.phrmafoundation.org</a></li> </ul>
<b>UCB/UNC/Duke/Hamner Fellowship in Neurology and Clinical Drug Development</b>	<ul style="list-style-type: none"> <li>• Duration: 2 years</li> <li>• Provides clinical pharmacology and quantitative sciences didactic coursework; extensive hands-on training as an integrated member of UCB clinical development teams</li> <li>• Neuroscience specific</li> <li>• <a href="http://www.pharmacy.unc.edu/programs/fellowships/ucb-fellowship-in-neurology-and-clinical-drug-development">http://www.pharmacy.unc.edu/programs/fellowships/ucb-fellowship-in-neurology-and-clinical-drug-development</a></li> </ul>
<b>UC-SD Research Fellowship in Drug Development</b>	<ul style="list-style-type: none"> <li>• Duration: 2 years</li> <li>• Training occurs at UC-SD and industry partners</li> <li>• Neurologic and neurodegenerative diseases or CNS drug discovery tracks</li> <li>• <a href="http://pharmacy.ucsd.edu/faculty/research/fellowship-program.shtml">http://pharmacy.ucsd.edu/faculty/research/fellowship-program.shtml</a></li> </ul>
<b>UC-SF International Research Fellowship in Drug Development and Regulatory Science</b>	<ul style="list-style-type: none"> <li>• Duration: 2-3 years; US citizens or permanent residents only</li> <li>• Provides coursework in clinical pharmacology and trial design; strong mentored research component</li> <li>• Available focuses in drug development science, drug development science management, regulatory science</li> <li>• <a href="http://clinpharm.ucsf.edu/fellowship/">http://clinpharm.ucsf.edu/fellowship/</a></li> </ul>
<b>UNC/PPD Drug Development and Clinical Research Fellowship</b>	<ul style="list-style-type: none"> <li>• Duration: 2 years; US residents</li> <li>• Clinical research project at UNC during year 1; year 2 spent at PPD CRO</li> <li>• Coursework available in clinical pharmacology and clinical trial methodology</li> <li>• <a href="http://www.ppd.com/careers/academic_outreach/fellowships.htm">http://www.ppd.com/careers/academic_outreach/fellowships.htm</a></li> </ul>
<b>U Rochester Experimental Therapeutics Fellowship</b>	<ul style="list-style-type: none"> <li>• Duration: 2 years</li> <li>• Includes clinical subspecialty experience, didactic coursework, direct exposure to experimental therapeutic development, and independent research projects</li> <li>• Neuroscience specific</li> <li>• <a href="http://www.urmc.rochester.edu/neurology/training/experimental-therapeutics.cfm">http://www.urmc.rochester.edu/neurology/training/experimental-therapeutics.cfm</a></li> </ul>
<b>Course offerings</b>	
<b>American Course on Drug Development and Regulatory Sciences</b>	<ul style="list-style-type: none"> <li>• 6 intensive sessions (23 days) over 2 years</li> <li>• Training covers entire development lifecycle of a therapeutic</li> <li>• <a href="http://bts.ucsf.edu/acdrs">http://bts.ucsf.edu/acdrs</a></li> </ul>
<b>Drug Information Association</b>	<ul style="list-style-type: none"> <li>• Extensive catalog of online and live instructor trainings in United States and Europe; courses offered at annual meetings</li> <li>• Continuing education and certificate programs</li> <li>• <a href="http://diahome.org">http://diahome.org</a></li> </ul>
<b>Pharmaceutical Education &amp; Research Institute</b>	<ul style="list-style-type: none"> <li>• Wide variety of offerings from introductory drug development to focused courses such as regulatory and drug safety</li> <li>• Certificate programs available</li> <li>• <a href="http://Peri.org">http://Peri.org</a></li> </ul>
<b>Tufts Center for the Study of Drug Development</b>	<ul style="list-style-type: none"> <li>• 5-day postgraduate course in clinical pharmacology, drug development and regulation</li> <li>• Single-day roundtable forums and leadership course for drug development teams also available</li> <li>• <a href="http://csdd.tufts.edu/courses">http://csdd.tufts.edu/courses</a></li> </ul>

Abbreviations: CRO = contract research organization; PhRMA = Pharmaceutical Research and Manufacturers of America; SD = San Diego; SF = San Francisco; U = university; UC = University of California; UNC = University of North Carolina.

knowledge gained, they may also provide other benefits, such as added job opportunities for properly trained neurologists; networking and potential collaborations in clinical studies and other research projects; a larger pipeline of neurologists with drug development expertise that may encourage other trainees to consider training and working in therapeutic development; and a better understanding of the perspectives of the pharmaceutical industry and regulatory agencies.

**DISCUSSION** Clinical development is a challenging and potentially rewarding field offering several opportunities for neurologists. As therapeutic development in neurologic diseases expands, the need for neurologists with clinical development expertise continues to grow. Interested neurologists will benefit from specialized training, either as part of a focused fellowship experience or through other educational opportunities as outlined in this article. Finally, the participation of neurologists familiar with the clinical spectrum of neurologic diseases will enhance the scientific validity and clinical relevance of neurotherapeutics in development.

#### **AUTHOR CONTRIBUTIONS**

Jeffrey T. Guptill: conception, manuscript drafting and revision. O'Neill D'Cruz: conception, manuscript drafting and revision. Robert E. Dupuis: manuscript drafting and revision.

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