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Narrative Review: The Promotion of Gabapentin: An Analysis of Internal Industry Documents

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Background: Internal documents from the pharmaceutical industry provide a unique window for understanding the structure and methods of pharmaceutical promotion. Such documents have become available through litigation concerning the promotion of gabapentin (Neurontin, Pfizer, Inc., New York, New York) for off-label uses.

Purpose: To describe how gabapentin was promoted, focusing on the use of medical education, research, and publication.

Data Sources: Court documents available to the public from *United States ex. rel David Franklin vs. Pfizer, Inc., and Parke-Davis, Division of Warner-Lambert Company*, mostly from 1994–1998.

Data Extraction: All documents were reviewed by 1 author, with selected review by coauthors. Marketing strategies and tactics were identified by using an iterative process of review, discussion, and re-review of selected documents.

Data Synthesis: The promotion of gabapentin was a comprehensive and multifaceted process. Advisory boards, consultants meetings, and accredited continuing medical education events organized by third-party vendors were used to deliver promotional messages. These tactics were augmented by the recruitment of local champions and engagement of thought leaders, who could be used to communicate favorable messages about gabapentin to their physician colleagues. Research and scholarship were also used for marketing by encouraging "key customers" to participate in research, using a large study to advance promotional themes and build market share, paying medical communication companies to develop and publish articles about gabapentin for the medical literature, and planning to suppress unfavorable study results.

Limitations: Most available documents were submitted by the plaintiff and may not represent a complete picture of marketing practices.

Conclusion: Activities traditionally considered independent of promotional intent, including continuing medical education and research, were extensively used to promote gabapentin. New strategies are needed to ensure a clear separation between scientific and commercial activity.

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Recent litigation and congressional inquiry have provided access to pharmaceutical industry documents that shed light on the marketing strategies used to promote drugs (1). One example is the case of gabapentin (Neurontin, Pfizer, Inc., New York, New York). First approved by the U.S. Food and Drug Administration (FDA) in late 1993 for adjunctive treatment of partial complex seizures, by the mid- and late 1990s gabapentin was being widely used for the off-label treatment of pain syndromes and psychiatric conditions (**Figure 1**) (2–4). Although gabapentin was later approved for the treatment of postherpetic neuralgia, in 2004 the Pfizer subsidiary Warner-Lambert settled litigation and admitted guilt in connection to charges that during the 1990s it violated federal regulations by promoting the drug for pain, psychiatric conditions, migraine, and other unapproved uses (**Table 1**) (5–7).

Although news articles have described some practices used to market gabapentin (8, 9), to our knowledge there has been little systematic investigation of the overall structure of promotion for this drug. In this paper, we use public documents obtained through litigation to describe how marketing strategies and tactics for gabapentin were developed and used in the mid- and late 1990s. First, we describe the overall organization of marketing efforts, and how certain groups of physicians were targeted as recipients of and vehicles for promotion. Next, we describe specific marketing activities, focusing on how education, research, and other activities not typically considered promotional were used to achieve marketing goals.

Methods

We reviewed approximately 8000 pages of publicly available documents regarding the case of *United States of America ex. rel David Franklin vs. Pfizer, Inc., and Parke-Davis, Division of Warner-Lambert Company*. Among documents pertinent to this research, two thirds were created between 1994 and 1998 and comprised a mix of internal correspondence and reports; programs, presentations, and transcripts from activities sponsored by Parke-Davis; and correspondence between the drug company and outside vendors and physicians. The remaining pertinent documents included excerpted depositions of Parke-Davis employees and court documents. These documents are now available in a digital archive at http://dida.library.ucsf.edu.

We reviewed documents using the principles of grounded theory, an inductive approach in which source

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Key Summary Points

Industry promoted gabapentin for on- and off-label uses as part of a comprehensive marketing plan.

Frequent prescribers of anticonvulsant agents, opinion leaders, and local champions of gabapentin were specially targeted for promotion.

Gabapentin was promoted by using education and research, activities not typically recognized as promotional. "Independent" continuing medical education, "peer-to-peer selling" by physician speakers, industry-funded studies, and publications in the medical literature were used to advance marketing goals for the drug.

material was used to generate ideas rather than to test a preestablished hypothesis (10). All documents underwent primary review by 1 author, with selected review by the coauthors. First, we cataloged marketing techniques and identified broad themes about marketing strategy for gabapentin. Next, we discussed initial findings and re-reviewed pertinent documents in an iterative process to arrive at the final description and interpretation of marketing techniques and themes. To better understand the role of individuals and organizations discussed in the documents, we obtained supplemental information from the court and through Internet and PubMed searches.

Most data on payments to physicians and organizations were obtained from a payment register compiled by the plaintiff's attorneys from documents supplied by Parke-Davis (4, 11) and augmented with additional information provided to us by those attorneys (for additional detail on analyses of the payment register, see Appendix 1, available at www.annals.org). We also used budget planning documents from 1998 and other years to estimate expenditures for different forms of marketing (12–14).

During the period under review, gabapentin was approved only for the adjunctive treatment of partial seizures in persons older than 12 years of age at dosages up to 1800 mg/d. Thus, for this review, we considered any other indication to be unapproved. In quotations of documents, items in brackets are our addition and represent our best interpretation of abbreviations, phrases, and other data.

This research was approved by the Research and Development Committee of the San Francisco Veterans Affairs Medical Center and the Committee on Human Research at the University of California, San Francisco. The aforementioned archive paid the cost of obtaining and photocopying documents used in this research. No outside source had a role in the mechanisms of document review, presentation of results, or decision to submit the manuscript for publication.

DATA SYNTHESIS

Marketing Strategy

Each year, corporate leadership established broad goals ("strategies") for the marketing of gabapentin. Specific programs ("tactics") were then designed to achieve that year's strategic goals (15, 16). For example, planning documents for 1998 show a projected $40 million advertising and promotion budget for gabapentin organized under 4 "topline strategies," further divided into a variety of tactical categories (**Table 2**) (12, 13). Professional education accounted for half to two thirds of the projected promotional budgets for 1996 through 1998 (12–14).

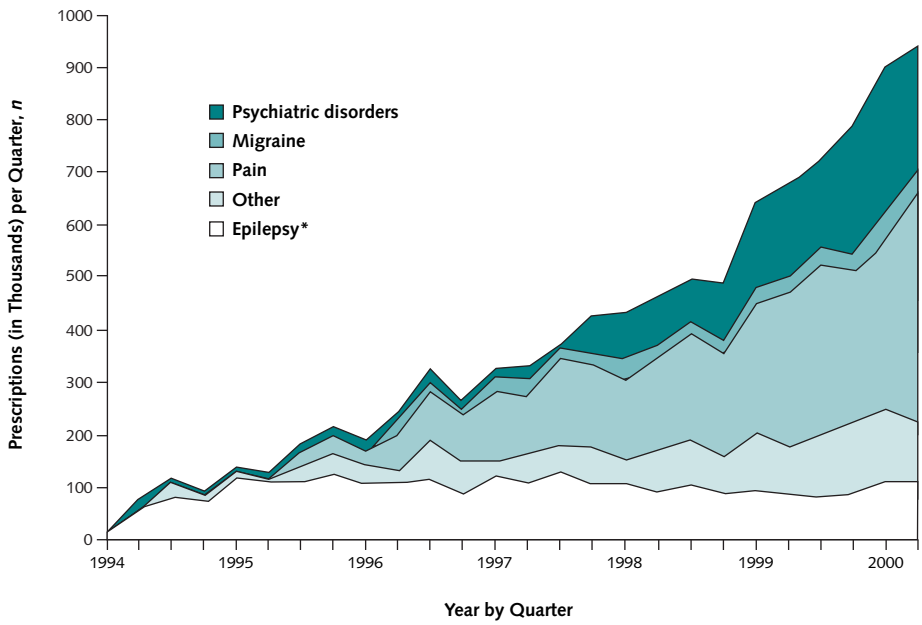
Parke-Davis identified several groups of physicians for targeted marketing. One such group was physicians who frequently prescribed anticonvulsant agents, categorized by the dollar value of anticonvulsant prescriptions they had the potential to generate (>$300 000 for the highest tier of prescribers) (14, 15, 17–23). Another key group was physicians who had the potential to influence gabapentin use among their colleagues. This included local champions of the drug, who were recruited and trained to serve as speakers in "peer-to-peer selling" programs (19, 24–26), which were noted to be "one of the most effective ways to communicate our message" (19). Another important segment was "thought leaders," "key influencers," and "movers and shakers," influential physicians identified in part by their affiliation with major academic medical centers (12, 13, 18–20, 24, 26–28). For example, in 2 documents Parke-Davis identified 40 potential thought leaders in the northeastern United States, including 26 current or future department chairs, vice chairs, and directors of academic clinical programs or divisions (24, 27). Of these 40 leaders, 35 participated in at least 1 Parke-Davis–sponsored activity, including 14 who requested or were allocated $10 250

Table 1. **Timeline***

Month and Year	Event
May 1977	U.S. patent for gabapentin granted to Warner-Lambert.
December 1993	FDA approves gabapentin for adjunctive treatment of partial complex seizures in patients age >12 y at dosages ≤1800 mg/d. Marketing exclusivity granted to Parke-Davis, a division of Warner-Lambert.
August 1996	Lawsuit filed by former Parke-Davis employee David Franklin alleging illegal marketing of gabapentin for off-label uses; case put under seal (action deferred pending government review).
December 1999	Seal on lawsuit lifted, litigation resumes.
June 2000	Warner-Lambert acquired by Pfizer.
October 2000	FDA approves gabapentin for adjunctive treatment of partial seizures in children age 3–12 y.
May 2002	FDA approves gabapentin for postherpetic neuralgia (in adults).
May 2004	Warner-Lambert admits guilt and agrees to pay $430 million in relation to criminal and civil liability regarding the promotion of gabapentin for uses not approved by the FDA.

* FDA = U.S. Food and Drug Administration.

Figure 1. **Prescriptions for gabapentin, by diagnostic category.**



Estimates of diagnosis-linked prescribing provided by Pfizer, Inc. (2–4). Each diagnosis was assigned to a diagnostic category by the authors. *Adjunctive treatment of epilepsy in adults older than age 12 years was the only U.S. Food and Drug Administration–approved use of gabapentin during the time period shown.

to $158 250 in honoraria, research grants, or educational grants between 1993 and 1997 (11).

Parke-Davis also targeted residents; planning documents for the 1998 advertising and promotion budget show allocations of $195 000 to $330 000 for "resident programs," a video case series, and a "CNS [central nervous system] residents course" (13). As described in one report, efforts with residents could be used "to influence physicians from the bottom up" and "to solidify Parke-Davis' role in the resident's mind as he/she evolves into a practicing physician" (24).

Tactics

Continuing Medical Education

"Medical education drives this market!!" noted the author of a Parke-Davis business plan (29). Accordingly, educational activities were used to implement strategic goals for gabapentin (12, 30–32), often through events at which physician speakers could communicate messages about gabapentin directly to their colleagues. Teleconferences linking paid physician moderators with small groups of physicians were a method for reaching prescribers. Although these teleconferences were titled as educational events (33), an internal memo about 1 set of 143 teleconferences on epilepsy management noted that "the key goal of the teleconferences was to increase Neurontin new prescriptions by convincing non-prescribers to begin prescribing and current prescribers to increase their new prescription behavior" (34). In some cases, Parke-Davis helped establish the agenda and was able to surreptitiously monitor teleconferences in progress. In 1 set of 39 calls organized through a medical education and communications company to discuss unapproved uses of gabapentin, an agenda was prepared for physician moderators directing them to discuss such topics as "how Neurontin evolved into a first line therapy option in your practice" (35, 36). In another series of "psychiatry" teleconferences organized through a third-party vendor, senior Parke-Davis employees were invited to participate but told to "instruct the teleconference operator that you should be in LISTEN ONLY mode and your name should NOT be announced during introductions" (capital letters in original) (37). Documents suggest that in some cases moderators were paid $250 to $500 per call and had other financial ties to Parke-Davis (11). For example, each of the 10 moderators from 1 series of calls requested or was allocated between $14 800 to $176 100 for participation in various Parke-Davis–sponsored activities between 1993 and 1997 (11, 33).

Speakers bureaus and related programs were other physician-to-physician activities developed to promote gabapentin (25, 26, 28, 38). Sales employees were encouraged to "expand the speaker base—identify and train strong Neurontin advocates and users to speak locally for Neurontin" (19). Parke-Davis also organized the Merritt-Putnam lecture series to improve "public relations within the neurology community, etc., as well as [to impact] the volume of Neurontin new prescriptions" (26, 28, 38). The speakers bureau for this lecture series included chairs of neurology departments and directors of clinical programs

at major teaching hospitals (11, 39). Members of the speakers bureau were invited to special meetings, where, in addition to lectures on the clinical use of gabapentin, they were updated on promotional strategies for the drug (39, 40).

Many educational events appear to have been sponsored directly by Parke-Davis. However, the company also funded educational programs through "unrestricted educational grants" to medical education and communications companies (hereafter termed "medical education companies"), for-profit businesses that specialize in producing conferences for physicians on behalf of pharmaceutical manufacturers and are often subsidiaries of marketing firms (41–44). Under this "unrestricted" arrangement, Parke-Davis officially relinquished control over program speakers and content. This allowed programs organized by medical education companies to discuss unapproved uses of gabapentin and to grant continuing medical education credit from the Accreditation Council of Continuing Medical Education (ACCME), neither of which is permissible for events directly sponsored by drug companies (45–48).

However, these same medical education companies also worked for Parke-Davis in several other roles, such as organizing teleconferences, coordinating advisory boards and consultants meetings, and conducting tactical planning to promote gabapentin (15, 17, 39, 47, 49–55). Because of these relationships, medical education companies had incentive to develop educational programs that were consistent with Parke-Davis's marketing goals and to control content in a way that reflected favorably on the sponsor (Appendix 2, available at www.annals.org) (56). For example, in 1996, one medical education company prepared a marketing proposal for Parke-Davis outlining 24 tactics to increase gabapentin use shortly after using an unrestricted grant from the drug company to organize a series of study programs on the use of antiepileptic agents for chronic pain (49, 57–59). Although the educational program prepared by this company was accredited by ACCME, Parke-Davis representatives were invited to a curricular development meeting (59), recruited physicians to participate in the course (60), and followed attendance counts at each program meeting (57). These actions were consistent with a Parke-Davis report that described the program as a tactic to support "growth opportunity" in off-label use (32). In another case, another medical education company that organized consultants meetings for Parke-Davis received a grant to assemble and train speakers to deliver grand rounds lectures on anticonvulsant use in nonepileptic conditions at approximately 70 community and teaching hos-

Table 2. **Draft Advertising and Promotion Budget for Gabapentin for 1998, by Strategy and Tactical Category***

Tactical Categories, with Examples†	Budget, in Thousands of Dollars‡				Total Budget in Thousands of Dollars
	Expand Neurontin Use in Epilepsy Monotherapy	Conduct Targeted Promotional/CME Efforts on High-Prescribing Physicians	Develop and Leverage Thought Leader Support	Maximize Opportunities in "Emerging [Unapproved] Uses"	
CBU/SPE	5300	1500	1600	0	8400
Professional education (e.g., speakers bureau, advisory boards, dinner meetings)	6229	0	1842	11 039	19 110
National speaker (e.g., physician honoraria and travel, speaker programs)	2110	500	550	0	3160
Direct mail	900	0	0	0	900
Professional promotional literature (e.g., convention giveaways, patient brochures)	2240	100	620	0	2960
Medical journal (e.g., journal advertising)	1200	0	0	0	1200
Gratis merchandise (e.g., patient assistance programs)	700	100	50	0	850
Samples	800	300	100	0	1200
Displays, agency fees, pack/ship, miscellaneous (e.g., convention displays)	1570	150	0	0	1720
Market research	400	0	0	100	500
Total	21 449	2650	4762	11 139	40 000

* The meaning of the term "CBU/SPE" is unclear, although "CBU" typically refers to "customer business unit," regional divisions of Parke-Davis. CME = continuing medical education.
† Tactical categories are listed as they appear in the source document (12). Examples were taken from line items in budget planning documents assigned to each category, although no specific examples were available for certain categories.
‡ Strategies were listed in budget planning documents as follows (12, 13): 1) "Expand Neurontin use in epilepsy through the introduction of monotherapy"—Parke-Davis had expected U.S. Food and Drug Administration approval for gabapentin as monotherapy for epilepsy, but the application was rejected; 2) "Conduct targeted promotional/CME efforts on high decile Neurologists & PCPs [primary care physicians] to increase their overall Neurontin usage"; 3) "Continue to develop and leverage thought leader support throughout the community to maintain our leadership position and achieve our business potential"; 4) "To maximize opportunities in the 'emerging [unapproved] uses' through clinical trials, publications, and educational events."

pitals across the northeastern United States (51, 61). Parke-Davis also sought to provide unrestricted educational grants to locally organized symposia at which it expected gabapentin to be favorably discussed (62). One memo recommended the following: "Assist in the organization of a [major university hospital's] pain symposium . . . .We will probably write them an unrestricted educational grant to help fund the project. In return, they will discuss the role of Neurontin in neuropathic pain, among other topics. They do have a very favorable outlook toward Neurontin" (63).

Unrestricted grants were used to underwrite other forms of education, including payments to physicians to cover the cost of attending conferences (64). Another grant exceeding $300 000 funded the production, printing, and distribution of 75 000 copies of an epilepsy handbook, with half of this budget allocated to soliciting interest among and delivering books to high prescribers of anticonvulsant agents (65).

Advisory Boards and Consultants Meetings

The stated purpose of advisory boards and consultants meetings was to solicit feedback from physician participants (47, 66). This objective was met at meetings where feedback was requested on clinical trial design (53, 67, 68), educational curriculum development (50, 67), and marketing strategies for gabapentin (14, 54, 67–69). However, other aspects of meetings were conducted in a manner more suggestive of promotional intent. For example, attendees at one consultants meeting were invited largely because of their high rates of anticonvulsant prescribing (17), and sales representatives were given "trending worksheets" to track prescribing behavior before and after the event (70); at the meeting, "participants were delivered a hard-hitting message about Neurontin" (71). Some meetings resembled educational conferences, with dozens of participants and an agenda dominated by lectures from physician "faculty" (17, 52, 71–73). Other meetings seemed to focus on cultivating relationships with thought leaders (26, 69), as in one meeting at which lecture notes for the regional business director notified attendees that "we would like to develop a close business relationship with you" (69).

Participants in advisory boards and consultants meetings received honoraria in addition to paid travel, lodging, and amenities at the resorts and luxury hotels at which such events were held (51, 52, 71–76). In addition, a number of faculty at these events received thousands of dollars in honoraria and grants from participating in these and other Parke-Davis activities (11, 52, 71, 73). These faculty may have been carefully vetted. As described by a medical education company that organized meetings, "it is [our] policy to complete a literature search to determine who authors favorable articles on the topics outlined" (56). In addition, the company reserved the right in nonaccredited programs "to probe the faculty further to definitively establish presentation content and make the appropriate changes and/or recruit an alternate speaker" (56).

Research Strategy and Publication

Research and publications on gabapentin served as key elements in the marketing strategy for the drug (26). For some clinical uses, such as monotherapy for epilepsy, research was used to support the company's attempt to obtain FDA approval for a new "on-label" indication. However, in other cases Parke-Davis employed a "publication strategy," the goal of which was to use research not as a means to gain FDA approval for new indications but "to disseminate the information as widely as possible through the world's medical literature" (77), generating excitement in the market and stimulating off-label prescribing despite the lack of FDA approval (78, 79). This strategy focused primarily on expanding gabapentin use in neuropathic pain and bipolar disorders, for which detailed decision analyses projected the greatest revenue potential (80–83).

The success of this strategy depended in part on publications being favorable to gabapentin. Some employees of Parke-Davis felt an obligation to publish studies with unfavorable results (80, 84), and in a number of instances such results were published (85–87). However, management expressed concern that negative results could harm promotional efforts (88), and several documents indicate the intention to publish and publicize results only if they reflected favorably on gabapentin (78, 79). As stated in a marketing assessment, "The results of the recommended exploratory trials in neuropathic pain, *if positive*, will be publicized in medical congresses and published" (italics added) (78). Similarly, in discussing 2 nearly identical trials that yielded conflicting results on gabapentin as seizure monotherapy, the "core marketing team" concluded that "the results of [the negative trial] will not be published" (89). (The positive trial was published [90], but we could not locate the negative trial on a PubMed search.)

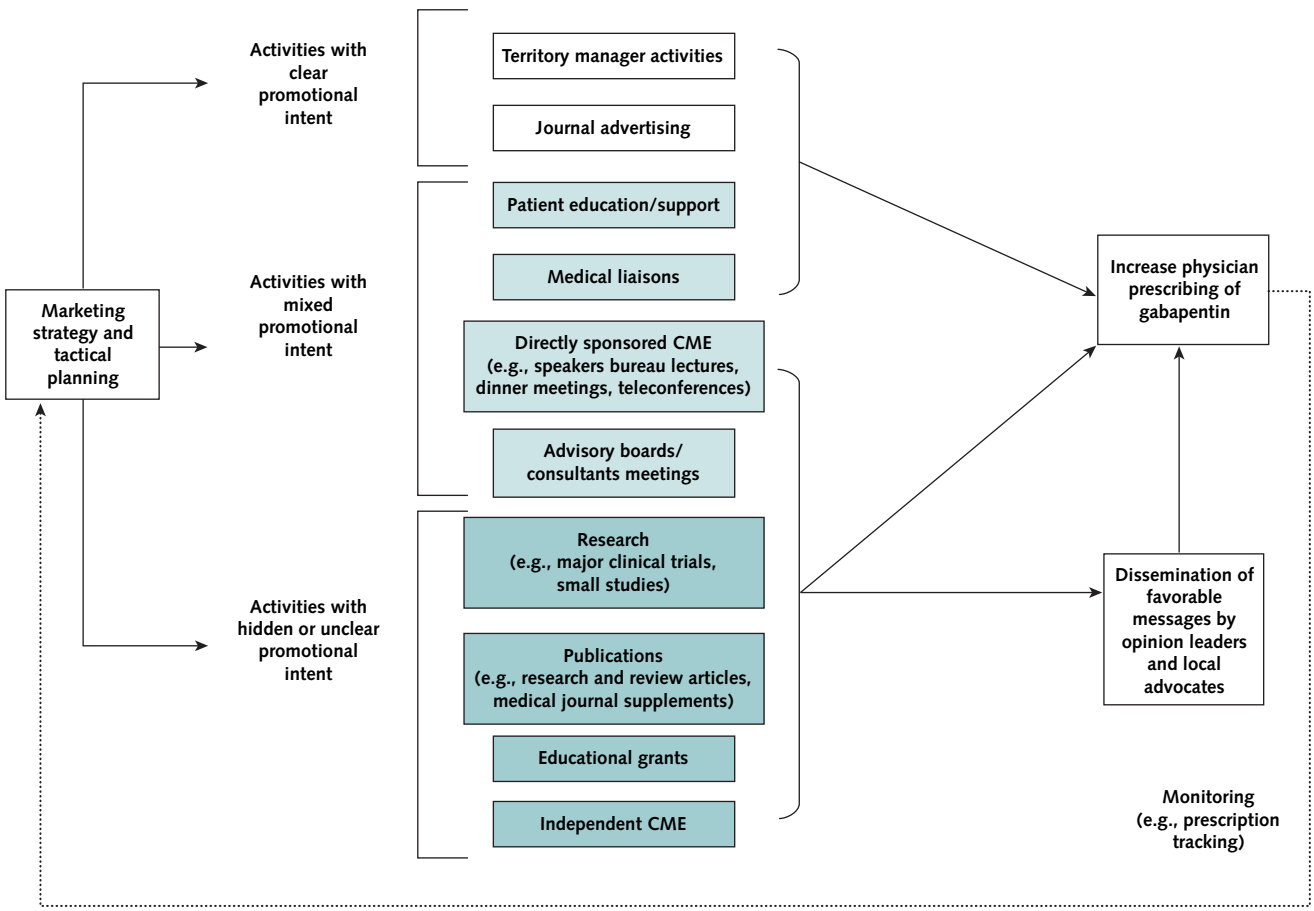
Beyond publishing its own clinical trials, Parke-Davis expanded the literature on gabapentin by contracting with medical education companies to develop review papers, original articles, and letters to the editor about gabapentin for $13 375 to $18 000 per article, including a $1000 honorarium for the physician or pharmacist author (91–98). For example, one "grant request" from a medical education company to Parke-Davis proposed a series of 12 articles, each with a prespecified topic, target journal, title, and list of potential authors (to be "chosen at the discretion of Parke-Davis") (96). This proposal noted that "all articles submitted will include a consistent message . . . with particular interest in proper dosing and titration as well as emerging [off-label] uses," mirroring Parke-Davis promotional goals for the drug (96). In this case Parke-Davis requested that authors prepare articles and submit them for peer review (92, 96). However, in another instance the medical education company offered substantial assistance in the development of manuscripts, reporting in a status

report that "at [the author's] request, we did an extensive literature search and submitted selected articles to him for reference . . . . We have offered him help in identifying and collecting his appropriate cases, analyzing data, writing a manuscript, or whatever he needs" (91). Among 7 published articles that we matched to sponsorship by a medical education company, 4 had favorable conclusions about gabapentin (99–102), and the other 3 adopted a neutral tone (103–105). Article sponsorship was often not disclosed, with 6 of 7 articles not acknowledging receipt of an honorarium from the medical education company (although 1 of these acknowledged support from Parke-Davis) (99–105). In 5 of 7 articles, the author identified by the medical education company had received funds from Parke-Davis for speaking engagements, consultants meetings, or other activities (11).

Engaging physicians in the research process had potential benefits for Parke-Davis beyond the publications themselves, providing an opportunity to engage thought leaders, reward key physician customers, or influence prescribing (20, 50, 67, 106–108). Marketing strategy documents stated that "the list of key influencers should be . . . kept aware of the availability of research opportunities in clinical trials" (24) and recommended the "funding of smaller studies . . . with our key customers for investigation of Neurontin and pain" (29). Among the 40 thought leaders described, 5 requested or were allocated research funding ranging from $32 000 to $75 000 per person (11, 24, 27).

One notable example of the confluence between promotion and research was STEPS (Study of Neurontin: Titration to Effectiveness and Profile of Safety), an uncontrolled open-label study in which physicians were in-

Figure 2. **Framework for gabapentin marketing.**



In this model, marketing strategy and tactical planning allocate resources to different types of activities. Activities are divided into 3 categories according to the extent to which their promotional intent is generally known to physicians (for example, in directly sponsored continuing medical education [*CME*], the pharmaceutical company is known to be the direct source of funding, but because the event is framed as an educational program, its promotional intent may be obscured). Each of these activities can directly influence prescribing by practicing physicians. In addition, activities in the lower half of the figure can also influence prescribing through physician-to-physician communication, in which opinion leaders and local gabapentin champions are directly or indirectly engaged to communicate favorable messages about gabapentin to their colleagues. Physician prescribing patterns and other outcomes are then monitored to assess the effectiveness of marketing tactics, which influences future marketing planning decisions. For the sake of simplicity, other relationships are not shown in this diagram. For example, many marketing tactics can work synergistically, such as the use of research findings to promote gabapentin in CME settings.

structed to begin adjunctive gabapentin therapy in their patients with epilepsy and to keep increasing the dose until their patients were seizure-free, or until a maximum dosage of 3600 mg/d (twice the maximum FDA-approved limit) was achieved (109). More than 700 physicians were enlisted to participate, enrolling an average of 3 patients each (with a $300 payment for each patient enrolled) (109–111). The published report of the study stated that it "examined the effectiveness of gabapentin" in this dose range (109). However, company documents described the goal of the study as to "teach physicians to titrate Neurontin to clinical effect" (112) and "to give neurologists the opportunity to titrate to higher doses (>1800 mg) when needed" (16), central promotional goals at the time (30, 69). Described as a "key activity" for the implementation and support of marketing goals, "indicators of success" for the study included increases in market share and use of higher doses of gabapentin (16, 30). At least 6 of 9 authors of the published report had substantial financial relationships with Parke-Davis; they had participated in a total of 263 activities sponsored by Parke-Davis between 1993 and 1997, with requested or allocated payments ranging from $11 450 to $69 000 per author (11, 109).

DISCUSSION

During the mid- to late 1990s, Parke-Davis used a comprehensive campaign to promote prescribing of gabapentin. Research, publications, and educational programs (including "independent" events) were used as marketing opportunities, augmented by opinion leaders and local physician champions to engage their physician colleagues. Since the promotional intent of these activities may not have been widely recognized, their impact on physicians was probably greater than interactions with known commercial intent, which are typically approached with greater skepticism (42, 43, 113–115).

While the limited nature of our source material precludes a definitive understanding of marketing practices, we hypothesize a model for the marketing of gabapentin that incorporates our findings (**Figure 2**). In this model, activities with clear promotional intent are known to originate from a pharmaceutical manufacturer and to serve a commercial purpose (thereby disclosing potential commercial bias). In other activities, the promotional underpinnings may be partially obscured (for example, where funding is known to originate from a drug company, but where the stated purpose of the event is education) or largely obscured (for example, "independent" activities delivered through a third party, or funding for research and publication). Many such activities rely on physician-to-physician communication, in which opinion leaders and local advocates are engaged with speaking, research, and educational opportunities and in turn may communicate favorable messages about the drug to their colleagues.

Our work has several limitations. First, our research was limited to publicly available documents, many of which were submitted by the plaintiff to support allegations of off-label marketing; as a result the view of company practices and decision making is incomplete. Second, we could not determine the frequency of specific activities, nor in most cases confirm that planned activities and payments were executed. Third, this report is based on primary document review by 1 investigator and collaborative interpretation of the authors, 3 of whom were unpaid expert witnesses in the litigation that yielded the documents. The reproducibility of our findings has not been established. Fourth, we reviewed the marketing practices for a single drug made by a single company, and we do not know the extent to which these techniques were used in the marketing of other products made by Parke-Davis or by other pharmaceutical firms. Finally, the litigation focused not on marketing activities themselves but on whether these activities were used to promote unapproved uses (5, 6). Thus, although certain activities, such as ghostwriting, violated prevailing ethical norms, many appear to have been legal (or in a broad "gray zone" of legality) when or if used solely to promote FDA-approved indications for gabapentin (48, 116, 117).

There is widespread agreement that commercial interests should not influence the clinical decisions that physicians make on behalf of their patients. As a result, a complex system has evolved to help manage these conflicts, focused primarily on disclosure and self-regulation by physicians, professional organizations, and the pharmaceutical industry. These efforts have been largely ineffective (118, 119), and the techniques used to promote gabapentin illustrate how commercial interests can intrude into the practice of medicine in both visible and hidden ways. Incremental efforts to strengthen the existing patchwork of guidelines are unlikely to be sufficient in an environment where marketing is so deeply embedded and where the borders between research, education, and promotion are more porous than is commonly recognized. New strategies are needed, including rigorous regulatory oversight, strict sequestration of commercial and scientific activities, and a fundamental internal reevaluation of the interactions between individual physicians, professional organizations, and industry (42, 120–124).

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Appendix 1: Analysis of the Payment Register

The payment register was assembled by the plaintiff's attorneys by using data from documents provided by Parke-Davis, in most cases covering 1993–1997. It was organized by individual physicians or institutions, with each payment to that individual, or activity attended by that individual without evidence of payment, appearing as a separate line in the spreadsheet. We used this register to assess payments to physicians of interest whom we identified by name in other court documents, such as physicians targeted as "thought leaders," or physicians who moderated teleconferences on behalf of Parke-Davis. For each physician of interest, 1 of the authors reviewed all line-item entries for that physician to eliminate duplicate entries. Then, on the basis of limited descriptive information for each line item, funds were classified as "requested" (for example, a letter from a physician requesting grant support) or "allocated" (for example, an agenda for an upcoming event with a notation of expected payment). In the absence of contrary evidence, most payments under $2000 were considered "allocated" since they usually appeared to be honoraria. However, in most cases we could not definitively confirm that physicians participated in or received payment for the listed activity.

Appendix 2: Control of Content in an "Independent" Program: A Case Study

In a letter from the medical education and communications company Proworx to Parke-Davis (56), the author describes working with Parke-Davis on an upcoming satellite symposium at the American Diabetes Association annual meeting. When employees at Proworx became concerned about possible "negative" content at their program, they took corrective action (surnames have been removed in the reproduction of this letter):

> When Proworx finally received each of the abstracts [for talks by two speakers] within the week prior to the actual program, they were immediately forwarded to both Vic and Allen [Parke-Davis marketing employees] for their comments. Upon receipt of Dr. B's abstract, Vic called Bina [a project director at Proworx] to express his concerns. However, Bina had already contacted [the accrediting institution] to establish what could be done, within the accreditation guidelines, to address these concerns. At that point, Dr. B. was contacted and told that the accrediting institution had asked that she revise her abstract to remove any specific product information that she could not provide references for. She then revised her abstract and faxed it back again for our review. Lisa, the copy writer for the Parke-Davis account, was then contacted and asked to make any further revisions.
>
> Although the abstract had been revised, there were still concerns on Proworx's and Vic's part in regard to Dr. B's presentation. Her abstract illustrated that [she] was clearly not planning on presenting what had originally been agreed upon. Therefore, Proworx immediately looked at what possible options were available, aside from canceling her talk, to counteract a possible 'negative' presentation. [The accrediting institution] was contacted to address accreditation issues and the CDM [Cline, Davis & Mann, an advertising firm that was the corporate parent of Proworx] account team met with Bina to identify what key issues needed to be presented to give attendees a 'positive message' to go away with.
>
> At this point, Proworx requested that Dr. B. forward a copy of her slides for our review. Upon review, we determined that the slides did not include any specific negative information in regard to Neurontin or anticonvulsants as a whole, and that we should concentrate on creating a setting in which she would have no choice but to address the issue she had originally agreed to present. Therefore, when meeting with the CDM account team, pre-written questions were developed to address any issues that were not mentioned in Dr. B's presentation, as well as questions counteracting negative comments . . . .
>
> It was then decided that the best option, while not crossing over [American Council of Graduate Medical Education] guidelines, was to present questions at the Q & A session, which would take place immediately following her presentation. This did indeed lead Dr. B. to address some of the positive aspects of anticonvulsants and of Neurontin . . . .
>
> If this had not been an accredited program, Proworx would have been able to probe the faculty further to definitively establish program content and make the appropriate changes and/or recruit an alternative speaker.