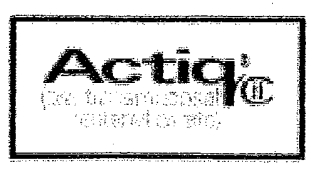




# 2005 ACTIQ® Marketing Plan

Andy Pyfer, Product Director; Paula Castagno, Sr. Product Manager;  
Terrence Terifay, Sr. Product Manager; Dean Robinson, Product Manager;  
Suzanne Richards, Promotions Marketing Associate



## Table of Contents

<b>I. Executive Summary</b>	<b>2</b>
<b>II. Situation Analysis</b>	<b>5</b>
A. 2004 Review	5
B. Sales and Prescription Update	8
C. Target Audience Analysis	14
D. Prescriber Base Analysis	20
E. Product Awareness Perception and Usage	23
F. Competition	26
G. Reimbursement Update	30
H. Medical Education	34
I. Promotional Activities	35
J. Market Dynamics	36
<b>III. SWOT Analysis and Key Marketing Issues</b>	<b>40</b>
A. ACTIQ SWOT Analysis	40
B. Key Marketing Issues	40
<b>IV. Product Vision and Positioning</b>	<b>45</b>
A. Product Vision	45
B. ACTIQ 2005 Positioning	45
C. Patient Profile	45
<b>V. Marketing and Promotional Strategy</b>	<b>46</b>
A. 2005 Objectives	46
B. Marketing Strategy	47
C. Critical Success Factors	52
<b>VI. Tactical Plan</b>	<b>55</b>
A. ACTIQ Key Messages	55
B. Target Audience	57
C. Core Tactical Plan	57
D. Sugar Free Launch Plan	60
E. ACTIQ 2005 Market Research Plan	62
F. Public Relations Plan Under Consideration	63
<b>VII. Appendix</b>	<b>67</b>

## I. EXECUTIVE SUMMARY

### 2004 Performance Review

In 2004, ACTIQ has continued its growth, however, not at the same rate as in prior years. ACTIQ sales for 2004 will likely fall short of the budget number of \$416 MM with a forecast number of \$387 MM in gross shipments. This represents growth of 52% over sales of \$254.4 MM in 2003. Prescription growth has also been slower than anticipated and prescriptions are expected to reach 439,969 or 83% of budget, representing 35% growth over 2003. This compares to the 76% growth rate seen from 2002 to 2003. A primary contributor to the shortfall in sales is due to a decline in the value of the prescriptions. Prescription value has declined due to a higher volume of new writers generating fewer prescriptions with fewer units per prescription.

Some factors that may have contributed to this slower growth include: external factors, internal factors, and also challenges inherent in the ACTIQ selling process.

#### External Factors:

- Negative media attention towards ACTIQ and opioids
- Increased scrutiny from law enforcement and regulatory agencies towards opioids
- DDMAC criticisms of promotional materials
- Growing “opiophobia” – fear of opioids by the medical community and patients suffering in pain
- Competitive counter-detailing of ACTIQ/BTCP
- Increasing reimbursement barriers

#### Internal Factors:

- Formulation change in Q3 2003 that was not initially well received by the medical community and existing patients
- Approx 80% of current sales force new to ACTIQ/pain market
- Competing demands on sales force time/effort
- Compliance standards
- Lack of adequate support and direction via PRC
- Lack of adequate support via Scientific Communications
- No response on possible WLF reprints
- Small marketing team – heavy workload

#### ACTIQ Specific Selling Challenges:

- Different delivery system – requires a change in the treatment paradigm
- Perceived cumbersome dosing and titration process
- Major education involved about BTCP, fentanyl, dosing, etc.
- Whole office and pharmacy sell
- CII medication requires additional effort by clinicians and pharmacies

### 2004 Results

- 2004 projected TRx of 439,969 (83% of budget)
- 2004 projected sales of \$387 MM (93% of budget)
- Units growing at 1% for first 6 months of 2004
- Units/Rx in decline (-.4% growth) in first 6 months of 2004
- Prescriber count has grown 42%, from 9,742 to 13,786 for MAT June 2004
- Productivity of new prescribers is 10 times less than current prescribers (6TRx / new prescriber vs. 64TRx / current prescriber)
- For MAT June 2004, ACTIQ increased its market share from 5% to 6%, while all the other branded products lost market share

### 2005 Commercial Objectives

ACTIQ will continue to be positioned as fentanyl in a unique delivery system providing the most rapid onset of analgesia of any non-invasive opioid available which makes it the ideal agent for BTCP or rapid onset pain. The commercial objectives for ACTIQ include the following:

- Achieve factory sales and TRx count targets
- Increase productivity among targeted physician segments
- Expand the ACTIQ prescriber base, especially among the most productive physician segments

2005	Gross Shipments	Demand Sales	TRx
<b>2005 TOTAL</b>	<b>\$ 450.0 MM</b>	<b>\$ 446.3 MM</b>	<b>668K</b>

### 2005 Key Marketing Issues and Strategies

The overall marketing strategy for 2005 will continue to build on the platform developed in previous years, which will be to raise awareness of BTCP and ACTIQ and differentiate ACTIQ from its competitors by educating clinicians about the core product benefits (rapid onset of analgesia, portability, convenience and patient controlled administration).

The key marketing issues facing ACTIQ in 2005 that must be addressed include providing the sales force with effective tools as well as providing them with optimal messages for key targets; ensuring a smooth transition to sugar free ACTIQ; increasing awareness in assessing and treating BTCP; and addressing the fears and concerns surrounding opioids. Also, growing managed care issues must be addressed as well as increasing and improving Key Opinion Leader (KOL) relationships.

### **2005 Tactical Summary**

ACTIQ marketing strategies will be executed through a variety of tactical initiatives that convey ACTIQ key messages and differentiate ACTIQ from its competitors based on its primary patient benefit, rapid onset of analgesia and pain relief. As in 2004, the majority of tactics will focus on continuing to develop the market for BTCP and ACTIQ. Initiatives focused on improving awareness of BTCP and ACTIQ will be utilized among both patient populations and clinicians. Both promotional and continuing medical education programs will be implemented in 2005 and will continue to comprise a critical component of the tactical plan. New in 2005 is *Emerging Solutions in Pain (ESP)* which is an initiative developed by physicians for physicians, pharmacists and other healthcare professionals, to address some of the most critical issues in pain management today. These issues involve balancing the fundamental rights of patients and clinicians with the challenge of identifying patients who are at greater or lesser risk for opioid misuse and addiction, and with the challenges associated with the complex regulations involved in prescribing controlled substances. *ESP* is a branded educational initiative owned by Cephalon, Inc in order to support the Risk Minimization Strategy Team (RMST) and the Pain Franchise.

## II. SITUATION ANALYSIS

### A. 2004 REVIEW

#### *2004 Marketing Objectives*

The 2004 marketing objectives were to achieve gross factory sales of \$416 MM and total prescriptions of 530,499. Additional objectives included:

- Increasing awareness of ACTIQ and BTCP among targeted physician specialties/segments and patient populations
- Increasing the overall number of ACTIQ prescribers
- Increasing the number of prescribers in the top five TRx and Units prescribing deciles (i.e. move prescribers along the product adoption curve from dabblers to users/adopters)
- Increasing ACTIQ prescriber productivity and prescriber retention
- Continuing to develop relationships with KOLs in pain management
- Developing a tool(s) to assist with managed care/Medicaid reimbursement
- Continuing to build on clinical data/publications initiated in 2003 to meet prescriber and advisor recommendations regarding:
  - Utilization data in various pain types/therapeutic applications
  - Simplified titration/dosing
  - Quality of life (improved patient functioning)

#### *2004 Marketing Strategy*

The primary ACTIQ marketing strategy in 2004 to achieve these objectives was to continue differentiating ACTIQ from its competitors by highlighting the primary product benefit: rapid onset of analgesia and pain relief. This strategy has not changed over the last several years and will again be the central focus in 2005.

#### *2004 Promotional and Educational Strategies*

The following specific promotional and educational supporting strategies directly addressed each of the key marketing issues identified for 2004.

- Educate key targeted physician specialties and patient populations about the importance of assessing BTCP and the benefits of treating it with ACTIQ
- Strengthen the association of ACTIQ and its key patient benefits through improved awareness and medical education
- Build/renew relationships with KOLs in pain management and targeted physician specialties through consultant meetings, advisory boards and PR efforts
- Support the direction of phase IV research and publication efforts to be consistent with commercial needs
- Proactively position ACTIQ to defend its market share against future branded competition
- Provide a mechanism to facilitate physician needs for appropriate and safe opioid prescribing habits
- Motivate and focus selling efforts on ACTIQ by providing quality selling tools, solid sales targets and passion for the product

- Fully assess and evaluate any lingering negative reaction to the compressed powder formulation and develop a plan of action to address/correct it

Overall, the marketing initiatives implemented in 2004 have been adequately executed and sales and prescriptions continue to grow, however, not at the same level of growth as in previous years. Some factors that may have contributed to this slower growth include: external or environmental factors, internal factors, and challenges inherent in the ACTIQ selling process.

**External Factors:**

- Negative media attention
  - There has been an increase in the volume of press coverage around ACTIQ and other opioids. This coverage is centered mainly on cases of abuse and diversion.
- Increased scrutiny from law enforcement and regulatory agencies
  - Multiple meetings with states Attorneys General to discuss use of ACTIQ.
  - FDA has increased vigilance around ACTIQ promotional activities.
- DDMAC criticisms of promotional materials
  - New promotional items have been delayed or blocked, while current items have received new criticisms.
- Growing “opiophobia”
  - Concerns of abuse/addiction/diversion among physicians, patients and members of the general public.
  - Concerns with increased prescriber scrutiny. Physicians are under increasing pressure to properly evaluate patients and document their use of opioids.
- Competitive counter-detailing of ACTIQ/BTCP
  - Sales force reports of other representatives claiming their products are less abusable than ACTIQ
  - Long-acting opioid companies pushing clinicians to increase the dose or the frequency of the around-the-clock medications to avoid BTP and use of short acting opioids
- Increasing reimbursement barriers
  - Public and private payers have continued to raise their efforts to block access to ACTIQ. This has been done by instituting measures (e.g. prior authorizations) that either directly deny patient access to ACTIQ or increase the burden on patients and physicians to obtain reimbursement.

**Internal Factors:**

- Formulation change in Q3 2003
  - In July of 2003, ACTIQ changed to a compressed powder formulation, and the first few months post launch provided tremendous negative responses from both patients and clinicians as evidenced by the increase calls into our Professional Services line. From January to June 2003, the average calls

per month were 176. The calls for July, August, and September were 528, 1,109, and 876 respectively. This change to compressed powder formulation continued to have a negative effect on ACTIQ sales in early 2004, however, it has leveled off.

- Approximately 80% of current sales force/sales management team new to ACTIQ/pain market
  - Majority of Cephalon sales force needed to learn both the pain market, as well as the multiple aspects of the ACTIQ “full office” sell (physician, nurse, pharmacist, etc.).
- Competing demands on sales force time/effort
  - In 2004, the Cephalon sales force was tasked with selling all 3 promoted products, all of which have their own unique challenges. This may have limited the amount of time and/or quality of ACTIQ promotional efforts.
- Evolving compliance standards
  - Compliance standards continued to evolve in 2004 necessitating multiple and on-going improvements in all activities. Cephalon strives to remain in compliance in all aspects of promotion.
- Lack of adequate support and direction via PRC
  - Marketing has at times not received sufficient support or guidance resulting in delays in appropriate sales force support.
- Lack of adequate support via Scientific Communications
  - A pain-focused expert has not yet been hired.
- No response on possible WLF reprints
  - Marketing has been waiting for over 12 months for guidance regarding three WLF reprints. This has caused marketing to avoid suggesting additional reprints for WLF dissemination.
- Small marketing team – heavy workload

#### ACTIQ Selling Challenges:

- “Requires more time, effort, handholding” (a direct quote by an RSD)
- Different delivery system
  - A change in the treatment paradigm; different than taking a pill
- Perceived cumbersome dosing and titration process
  - Limited resources to educate about titration
  - Dosed in micrograms, most other pain meds are in milligrams
- Major education involved
  - Clinicians must first recognize and treat BTCP
  - Clinicians must understand fentanyl
  - Clinicians must understand why ACTIQ and its delivery system are a benefit to their patients
  - Clinicians must understand how to dose and titrate (relative potency)
- Whole office and pharmacy sell
  - Other office personnel (nurses, PAs, NPs) must understand how ACTIQ works and how to educate patients on using ACTIQ



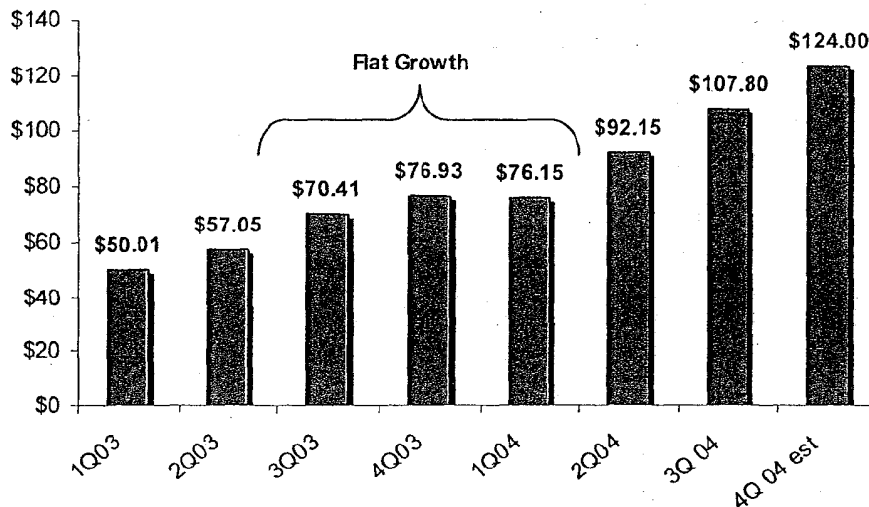
- Clinicians and office staff must understand and educate patients and caregivers on safe storage and disposal of ACTIQ
- Pharmacists must be comfortable storing and dispensing ACTIQ
- CII medications
  - Buys accompanying external issues (pharmacies must be approved to stock, clinicians must be savvy in patient selection and monitoring for opioid abuse, stigma attached to opioids, etc)
- We are lone promotional voice in the pure SAO market (a highly genericized marketplace)

**B. SALES AND PRESCRIPTION UPDATE**

**2004 ACTIQ Factory Sales**

In addition to the external/environmental challenges described, two specific internal events impacted ACTIQ sales in early 2004. First, in Q3 2003, ACTIQ changed from a cooked sugar to a compressed powder formulation. Second, in Q4 2003, Cephalon merged the PCS (79) and CNS (196) sales forces as well as expanded the entire sales force by the beginning of 2004 to a total of 435 representatives promoting all three Cephalon products. These two internal changes may have significantly contributed to a flattening of ACTIQ factory sales in Q4 2003 and Q1 2004. Growth resumed in Q2 2004, albeit not at the same rate as was seen immediately prior to these significant occurrences.

**Actiq Factory Sales by Quarter (MM\$)**

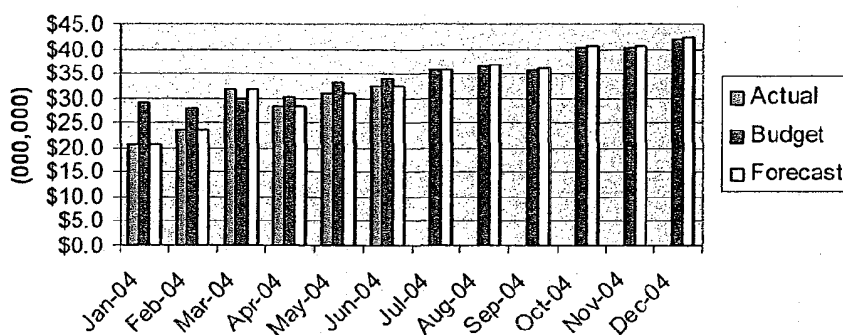


Source: SPS

**2004 ACTIQ Factory Sales versus Budget and Forecast**

The 2004 ACTIQ factory sales budget was \$416. Based on actual numbers to date for 2004, it is likely that ACTIQ sales may end up at \$387 MM (93% of budget). This is due to flatter than expected first and second quarter sales.

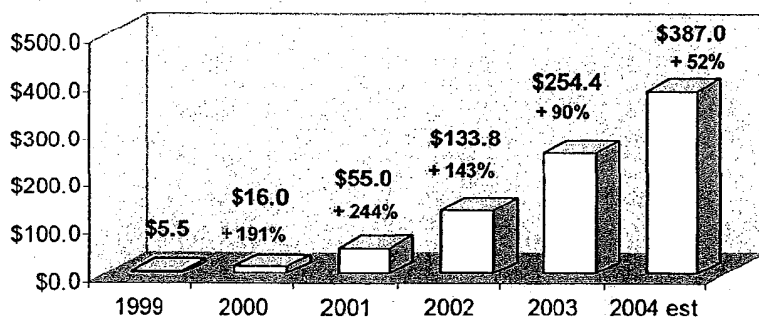
**ACTIQ Factory Sales vs Budget & Forecast**



Source: SPS

Assuming the factory sales come in at \$387 MM in 2004, although missing the budget number, this would represent growth of 52% over sales of \$254.4 MM in 2003. This growth rate is less than the growth rate seen from 2002 to 2003 (90%).

**ACTIQ Factory Sales (MM\$)**

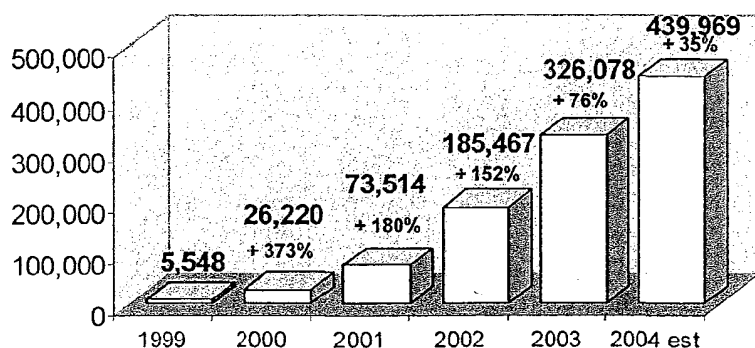


Source: DDN/SPS

**ACTIQ Prescriptions Since Launch**

Since the Cephalon launch in March 2001, ACTIQ prescriptions have achieved tremendous growth, in line with the sales growth since the 2001.

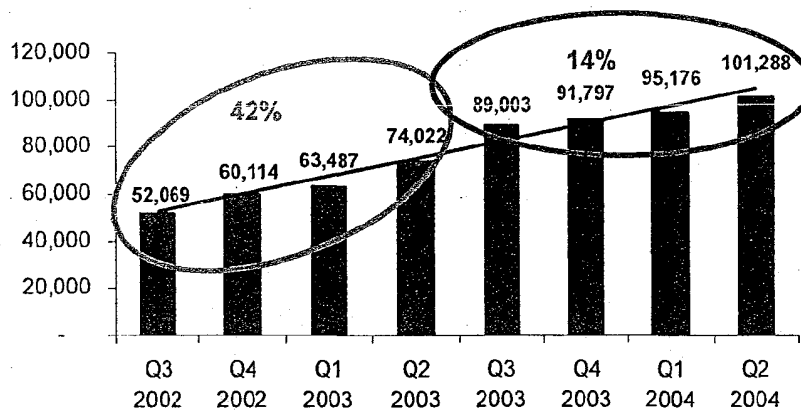
### ACTIQ Year on Year Prescription Growth



Source: IMS NPA

### 2004 ACTIQ Prescriptions

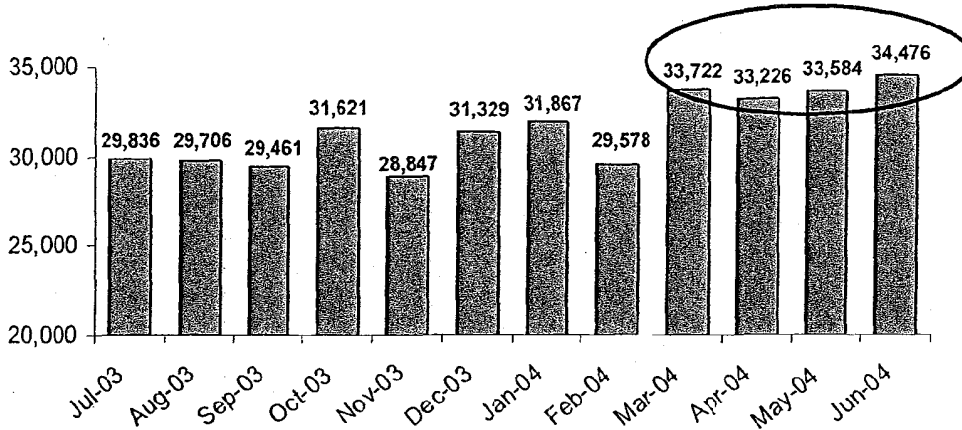
A quarterly look at ACTIQ prescriptions highlights the slower growth trend for 2004. The graph below shows 14% growth in the most recent four quarters through Q2 2004 as compared to the 42% growth rate for the previous four quarters.



Source: NDC Prescriber

The graph below illustrating TRx on a monthly basis shows relatively flat TRx over the last year and highlights the significant lack of growth over the most recent four month period (March – June 2004).

### ACTIQ Monthly TRx

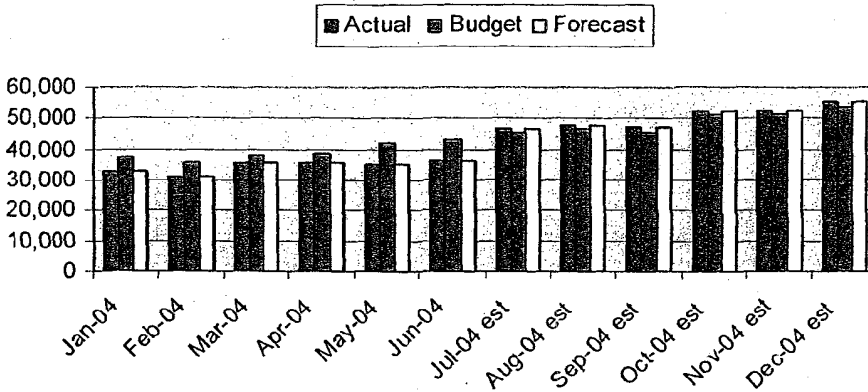


Source: NDC Prescriber

### 2004 ACTIQ Prescriptions Versus Budget and Forecast

The 2004 prescription budget was 530,499. Based on the ACTIQ team's projections, it is likely that ACTIQ will generate the forecast number of 439,969 prescriptions, or 83% of the budget.

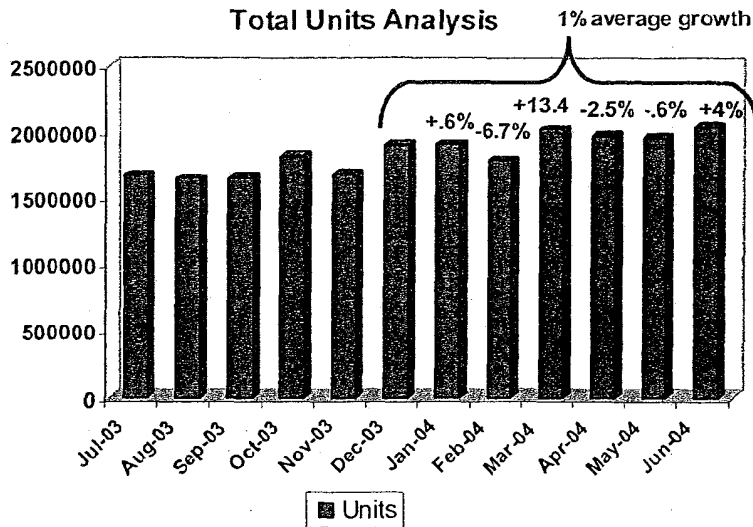
### ACTIQ Prescriptions vs. Budget & Forecast



Source: IMS NPA

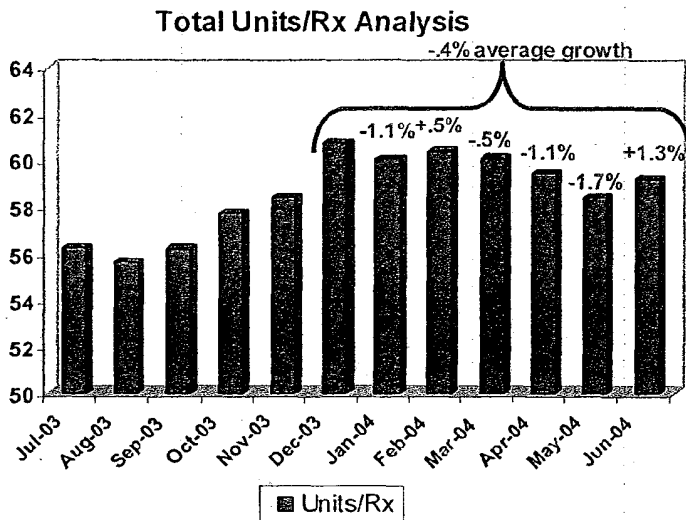
### Units and Units Per Prescription

The average unit volume for ACTIQ from July to December 2003 was 1.7 million units, growing 12% to an average of 1.9 million from January to June 2004. Despite this increase in average unit volume, the monthly growth rate has remained flat (1%) since January 2004.



Source: NDC Source Prescriber

One of the drivers of the value of a prescription is the prescription size - more units/TRx make for a more valuable TRx. For the first half of 2004, units/TRx were declining, likely due to the increase in new prescribers writing small titration prescriptions for new patients.



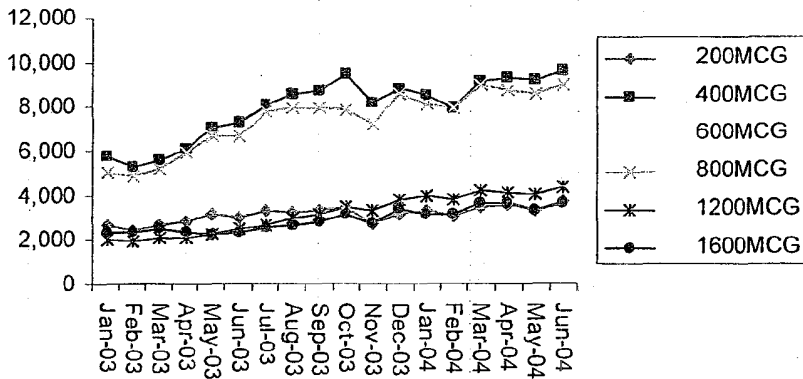
Source: NDC Source Prescriber

In summary, both sales and prescriptions will miss the budget numbers, with prescriptions falling shorter than sales. Fewer prescriptions than expected were generated and the smaller prescription sizes make for less valuable TRxs contributing to the shortfall in sales. Lastly, gross shipment performance is superior to TRx performance (and demand sales) due to adjustments (increases) in inventory.

**Prescription Count by Strength**

As mentioned, the prescription growth rates have slowed down in 2004. The monthly ACTIQ prescriptions by strength, shown below, declined during the fourth quarter of 2003, likely due to lingering negative reaction to the new formulation as well as the sales force restructuring. The first half of 2004 has shown a slight recovery from the fourth quarter levels. However, it is important to note that the volume of ACTIQ prescriptions is just now recovering to October 2003 levels.

**ACTIQ Monthly TRx by Strength**



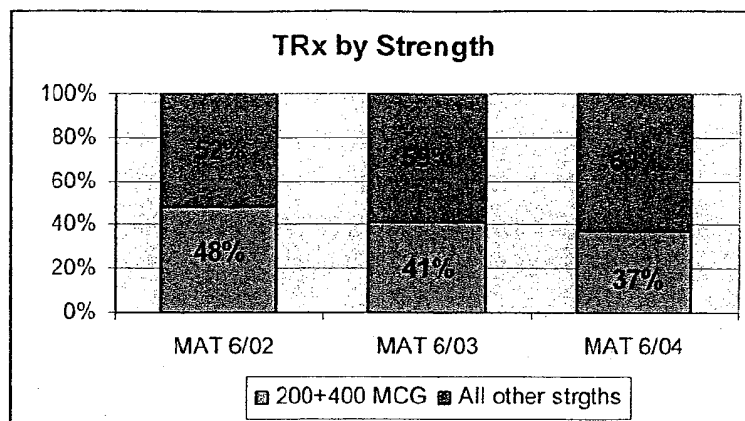
Source: IMS NPA

The 200mcg and 400mcg strengths of ACTIQ are generally used as indicators of new patient starts or titration prescriptions, which will likely turn into future, maintenance prescriptions. The growth rate of 200mcg and 400mcg prescriptions has significantly slowed. Growth of both strengths from MAT June 2002 to 2003 was 69%, while growth from 2003 to 2004 was only 44%.

	TRx MAT June 2002	TRx MAT June 2003	% growth	TRx MAT June 2004	% growth
200MCG	19,755	31,032	57%	39,903	29%
400MCG	40,239	70,310	75%	105,904	51%
	59,994	101,342	69%	145,807	44%

Source: IMS NPA

Also, as a percentage of all strengths, the 200mcg and 400mcg prescriptions have declined from 48% in 2002 to 37% in 2004. Not only will a lack of new starts affect 2004, but it may also have a significant impact on 2005.



### C. TARGET AUDIENCE ANALYSIS

#### *Target Audience Defined*

The ACTIQ targets include oncologists, pain specialists and selected physicians skilled in the use of opioids with the potential to treat cancer pain. General surgery, pediatricians and dentists are always excluded as targets due to ACTIQ contraindications, and prescribers who solely prescribe combination opioid products (such as Percocet, Vicodin, and Lortab) are excluded as targets as they are deemed less skilled in the use of opioids.

A formal three step process is used to determine targets.

- First: targets are evaluated based on opioid prescribing to determine skill level of opioids
- Second: specialties who are not likely to or do not have the potential to treat cancer (based on primary market research and other research reports) are excluded
- Third: specialties who write ACTIQ, but would fall outside of an ACTIQ appropriate target are flagged in the SMART database with an "S" for safety targets

Steps one and two result in the ACTIQ A and B targets. Below are the parameters used to determine the ACTIQ A and B targets.

#### **ACTIQ Tier A Targets**

11,588 prescribers were identified as ACTIQ Tier A Targets based on the following criteria:

1. ACTIQ Prescribers who wrote more than 5 ACTIQ TRx and more than 23 Total Opioid TRx.
2. Long Acting Opioid Prescribers greater than Decile 8 who wrote more than 23 Total Opioid TRx.
3. Pure Short Acting Opioid Prescribers greater than Decile 8 who wrote more than 23 Total Opioid TRx.

4. Prescribers who were a Long Acting Opioid Decile greater than 4 and a Pure Short Acting Opioid Decile greater than 2, wrote more than 23 Total Opioid TRx.
5. Prescribers who were a Pure Short Acting Opioid Decile greater than 4 and a Long Acting Opioid Decile greater than 1, wrote more than 23 Total Opioid TRx.
6. Duragesic Prescribers greater than Decile 5 who wrote more than 23 Total Opioid TRx.
7. In addition to meeting the prescribing-level criteria in lines 1-6 above, prescribers must have an ACTIQ-Approved Specialty.
8. Prescribers in the DDS, GS, or PD specialty groups or prescribers with a title of DDS or DMD are always excluded.

#### **ACTIQ Tier B Targets**

16,657 prescribers were identified as ACTIQ Tier B Targets based on the following criteria:

1. ACTIQ Prescribers who wrote at least 1 ACTIQ TRx.
2. Long Acting Opioid Prescribers greater than Decile 7 who wrote more than 23 Total Opioid TRx.
3. Pure Short Acting Opioid Prescribers greater than Decile 3 who wrote more than 23 Total Opioid TRx.
4. Prescribers who wrote greater than 6 Pure Short Acting Opioid TRx and are a Long Acting Opioid Decile greater than 1, wrote more than 23 Total Opioid TRx.
5. Duragesic Prescribers greater than Decile 3 who wrote more than 23 Total Opioid TRx.
6. In addition to meeting the prescribing-level criteria in lines 1-5 above, prescribers must have an ACTIQ-Approved Specialty.
7. Prescribers in the DDS, GS, or PD specialty groups or prescribers with a title of DDS or DMD are always excluded.

In addition to identifying the ACTIQ Tier A & Tier B Targets, Cephalon has also identified any ACTIQ prescribers who do not have an ACTIQ-approved specialty. These prescribers have been flagged as "Safety Targets" and marked with an "S" in the Smart database with the intent that they will be called on to receive ACTIQ messages regarding safety.

#### **ACTIQ Safety Targets**

1,321 prescribers were identified as ACTIQ Safety Targets based on the following criteria:

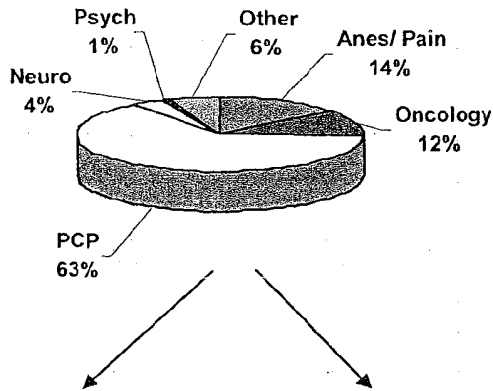
1. ACTIQ Prescribers who wrote at least 1 ACTIQ TRx.
2. Long Acting Opioid Prescribers greater than Decile 7 who wrote more than 23 Total Opioid TRx.
3. Pure Short Acting Opioid Prescribers greater than Decile 3 who wrote more than 23 Total Opioid TRx.



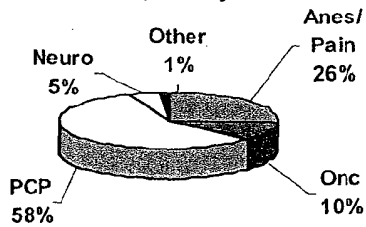
4. Prescribers who wrote greater than 6 Pure Short Acting Opioid TRx and are a Long Acting Opioid Decile greater than 1, wrote more than 23 Total Opioid TRx.
5. Duragesic Prescribers greater than Decile 3 who wrote more than 23 Total Opioid TRx.
6. Those physicians meeting the prescribing-level criteria in lines 2-5 above must also have an ACTIQ-Approved Specialty.
7. Prescribers in the DDS, GS, or PD specialty groups or prescribers with a title of DDS or DMD are always excluded.

The ACTIQ target list totals 29,566 – which equates to about 50-70 ACTIQ targets per TSS.

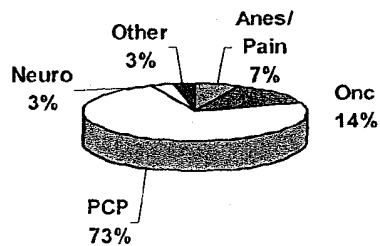
**Marketing Designated Targets by Specialty  
29,566 Physicians**



**Marketing Designated Targets  
by Specialty  
Tier A - 11,588 Physicians**



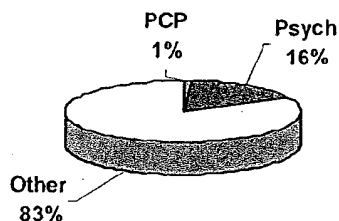
**Marketing Designated Targets  
by Specialty  
Tier B - 16,657 Physicians**



Source: NDC Source Prescriber

Below are the safety targets by specialty.

Marketing Designated "Safety" Targets by Specialty  
1,321 Physicians



Source: NDC Source Prescriber

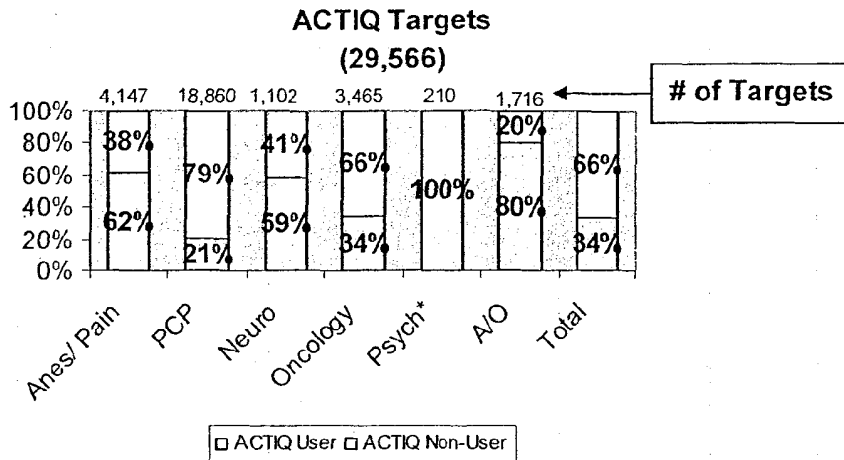
In addition to the targeting methodology, the TSS also use an algorithm to open each sales call. For A and B targets they open with a discussion of BTCP or with a discussion of breakthrough pain leading to BTCP and follow with the indication; or they state the approved indication for ACTIQ up front. In all cases they then inquire if the physician has the potential to treat cancer patients. For ACTIQ prescribers outside the targets and for non ACTIQ targets, all calls start with the TSS asking if the physician has the potential to treat cancer patients.

Once the TSS have screened each physician, they are trained to respond appropriately – either promoting or not promoting ACTIQ - depending on the physician response. Safety targets will always receive the ACTIQ safety messages.

The sales training department has these promotional guidelines on file.

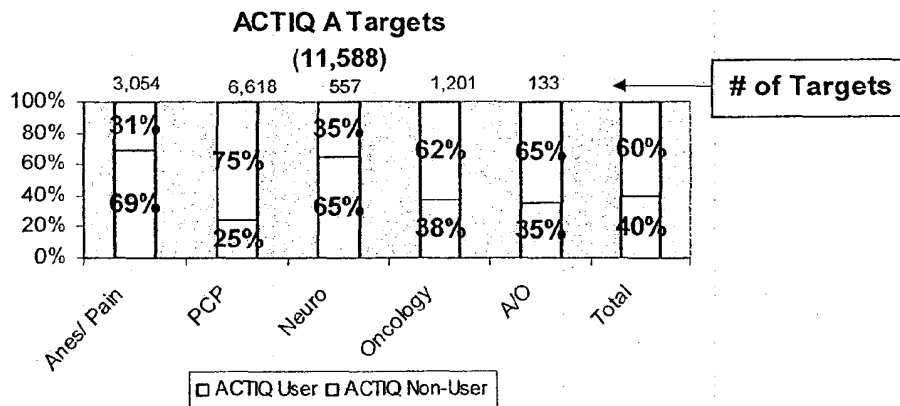
***Opportunity within Target Audience***

Of the 29,566 ACTIQ targets, 34% are ACTIQ users. (A user is defined as any prescriber who has written at least 1 ACTIQ TRx in MAT July 2004.) This leaves 66%, or 19,550 targets, with the potential to become ACTIQ users. Below are the total targets by specialty showing user versus non-user.



\*Note: The 210 Psych targets are all Safety targets.  
Source: NDC Source Prescriber

The A targets are generally believed to have the greatest potential among all targets. Of the 11,588 A targets, 40% are currently ACTIQ users, leaving 60% with the high potential to be ACTIQ users. Below are the A targets by specialty showing user versus non-user. This indicates good progress in penetrating the targets most likely to be receptive to the ACTIQ messages, yet there is still opportunity to grow.



Source: NDC Source Prescriber

**Users – Comparison of New versus Current Prescribers**

Of the total 29,566 ACTIQ targets, 34% are already using ACTIQ. Of those users, 42% are current users and 58% are new users. A current user is defined as starting to write ACTIQ in July 2002 and a new writer is defined as starting to write ACTIQ in July 2003. It is important to look at new versus current users because their productivity is different, as shown below. The majority of writers are new (58%) and they are much less productive than current writers, generating 8 prescriptions per prescriber versus 73 prescriptions per prescriber. This has been a factor in the slower than expected prescription growth. Prescriber productivity will be explored further in the prescriber analysis section.

	<b>TRx/Prescriber</b>
<b>New</b>	7.8
<b>Current</b>	73.2

**Non-users**

Although 66% of the total 29,566 targets have already met the ACTIQ target criteria and have the potential to become ACTIQ users, they have not yet done so. This may represent a significant area of opportunity but to establish the actual opportunity, additional analyses are needed. These analyses include segmenting the targets or looking at another indicator of behavior, such as opioid prescribing, as a marker to compare the users to the non-users.

**2005 Targeting Plans**

Historically, we have identified AB targets based on prescribing behavior and provided those to the field. Within those targets, emphasis in previous years has been based on specialty, with the most recent year looking more toward PCPs.

In 2005, we will be working towards further segmenting the AB targets to identify the next highest potential for ACTIQ writing, and clearly identify the messages that need to be placed against these groups. Several analyses on secondary data have been completed to identify the highest potential AB targets (see appendix 1), and include:

- 1) segmenting physicians based on high SAO use and high Duragesic use (both > 47 TRx)
- 2) segmenting physicians based on high SAO use and high LAO use (both > 47 TRx)
- 3) segmenting physicians based on high SAO use and high Oxycontin use (both > 47 TRx)

Within these analyses we have identified 920 physicians (excluding safety targets) who are ACTIQ users but who have received less than 1 call by a TSS. Our goals here are to increase promotional efforts (direct and non-direct) to increase their productivity. We will measure and monitor activity against this group.

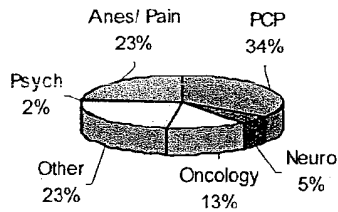
We have also identified 3,725 non-users who exhibit similar prescribing behavior to current ACTIQ writers. Our goals are twofold: Identify these physicians for the TSS and redirect promotional efforts against this group immediately. We will also conduct further market research to better understand motivations, perceptions and potential messages that will move this group from a non-user to a user. We will monitor this group closely.

**D. PRESCRIBER BASE ANALYSIS**

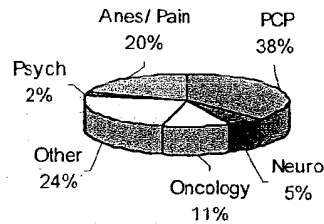
***Total Prescriber Count***

The total ACTIQ prescriber count for MAT June 2004 was 13,786, up from 9,742 in MAT June 2003, and all specialties have grown. Pain specialists and opioid-skilled PCPs continue to comprise the largest segments of the ACTIQ prescribing base at 20% and 38% respectively for MAT June 2004. Promotional and educational initiatives have also been focused toward oncologists, another growing segment, although it represents a smaller proportion of the total prescribing base. The segment labeled “Other” is comprised of many varied specialties writing small amounts of ACTIQ, none greater than 2% of the prescribing base.

**ACTIQ Percent of Prescribers by Specialty**  
**MAT Jun 2003**  
 (Total Prescribers = 9,742)



**ACTIQ Percent of Prescribers by Specialty**  
**MAT Jun 2004**  
 (Total Prescribers = 13,786)

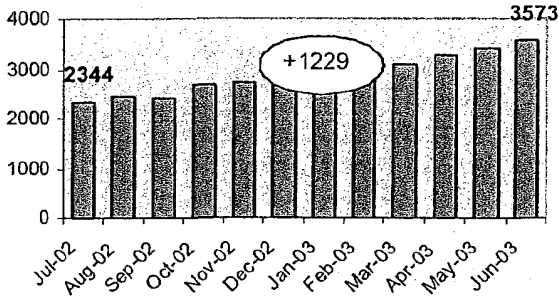


Source: NDC Source Prescriber

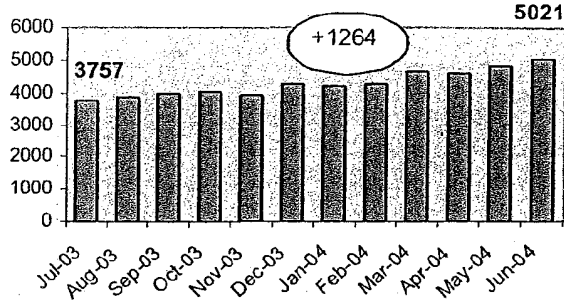
***Monthly Prescriber Count***

The number of unique monthly ACTIQ prescribers grew by 1,229 prescribers from July 2002 to June 2003, and by 1,264 from July 2003 to June 2004. Although sales and prescription growth has been sluggish, the number of new prescribers has continued to grow.

**ACTIQ Monthly Prescriber Count  
July 2002 - June 2003**

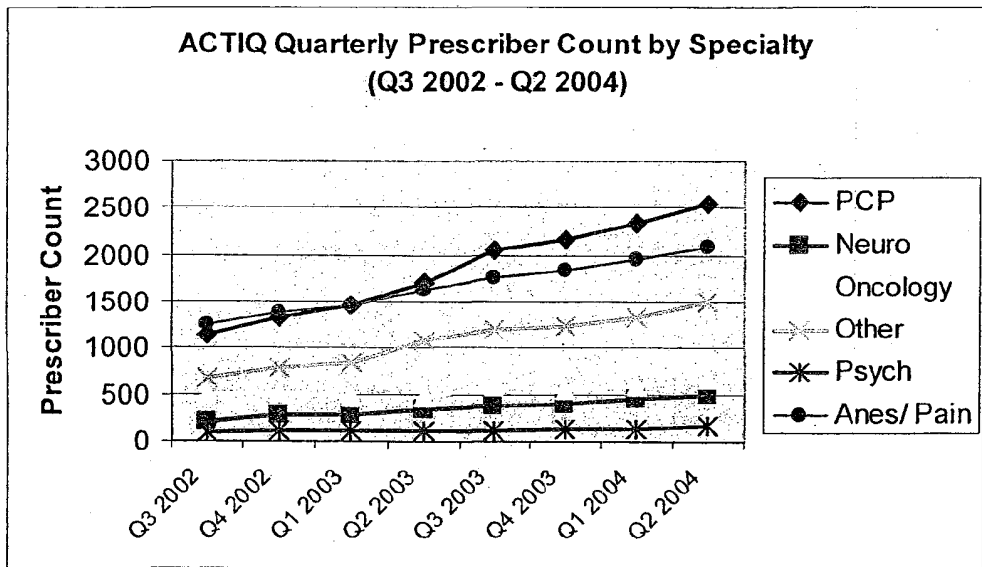


**ACTIQ Monthly Prescriber Count  
July 2003 - June 2004**



Examination of prescriber count by specialty over the most recent four quarters ending Q2 2004 shows growth among all specialties, specifically pain specialists and opioid-skilled PCPs – the two largest segments. Despite this growth in prescriber count, commensurate growth in prescription volume has not occurred. This may be due to these new prescribers being less productive. A prescriber productivity analysis follows.

**ACTIQ Quarterly Prescriber Count by Specialty  
(Q3 2002 - Q2 2004)**

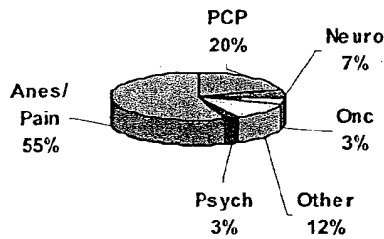


Source: NDC Source Prescriber

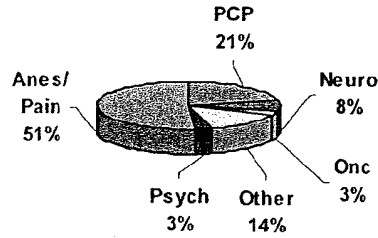
**Total Prescriptions and Productivity by Physician Specialty**

Pain specialists, historically the most productive specialty group, contributed the most prescriptions at 192,533 TRx for MAT June 2004 (51% of the 377,253 total prescriptions). This represents 40% growth in actual prescriptions over the previous period. Note that all specialty groups displayed growth in actual prescriptions over this time period, despite the change in their percentage of the total.

Percent of TRx by Specialty  
MAT Jun 2003  
(249,681 TRx)



Percent of TRx by Specialty  
MAT Jun 2004  
(377,253 TRx)



Source: NDC Source Prescriber

***Total Prescriptions and Productivity for New versus Current Prescribers***

In 2004, it became important to look at productivity by new users and current users, in addition to looking at productivity by specialty. Below is a comparison of the productivity of new ACTIQ writers versus current ACTIQ writers. For comparison, current writers are defined as those who began writing ACTIQ in July 2002 and new writers are defined as those who began writing in July 2003.

As physicians become more comfortable with ACTIQ and recognize its value in their practice, they write more prescriptions. For MAT June 2004, across all specialties, the current writers are far more productive than the new writers generating 64 TRx/prescriber versus 6 TRx/prescriber. As mentioned before, the anesthesiologist/pain specialists are historically the most productive, and the difference between current and new is even more apparent in this segment. The 1,753 current anesthesiologist/pain specialists prescribing ACTIQ generated 179,503 prescriptions, while the 1,059 newly prescribing anesthesiologist/pain specialists generated just 13,037 prescriptions. In this specialty, the productivity of current writers is much higher at 102 TRx/prescriber than for the new writers at just 12 TRx/prescriber.

ACTIQ Current Prescribers MAT June 2004			
Specialty	Prescriber Count	Total TRx	TRx/ Prescriber
PCP	1,446	59,243	41
Neuro	333	25,960	78
Oncology	564	8,040	14
Other	813	38,178	47
Psych	108	11,252	104
Anes/ Pain	1,753	179,503	102
<b>Total</b>	<b>5,017</b>	<b>322,176</b>	<b>64</b>

ACTIQ New Prescribers MAT Jun 2004			
Specialty	Prescriber Count	Total TRx	TRx/ Prescriber
PCP	3,735	20,920	6
Neuro	390	3,317	9
Oncology	929	3,382	4
Other	2,481	13,534	5
Psych	175	887	5
Anes/ Pain	1,059	13,037	12
<b>Total</b>	<b>8,769</b>	<b>55,077</b>	<b>6</b>

Source: NDC Source Prescriber

So the expanded reach of the sales force has generated new prescribers, however, they are less productive than current prescribers. Is it to be expected, then, that these new prescribers will eventually act like the current prescribers and become as productive? And will they respond to the same messages as the current prescribers responded to? If not, what messages will they need to hear? To further segment the market to answer these questions, market research was conducted to combine behavioral information – such as prescribing of other opioids– with attitudinal information to help predict ACTIQ prescribing levels. The topline results identified four segments: *Advanceable Experts*, *Open and Understanding* (both likely to respond to ACTIQ messages), *Entrenched Experts* (less likely to respond to ACTIQ messages), and *Addiction Concerned* (unlikely to respond to ACTIQ messages). Further message testing will be conducted and rollout and training are planned for the 2005 national sales meeting.

## E. PRODUCT AWARENESS, PERCEPTION AND USAGE

### *Awareness*

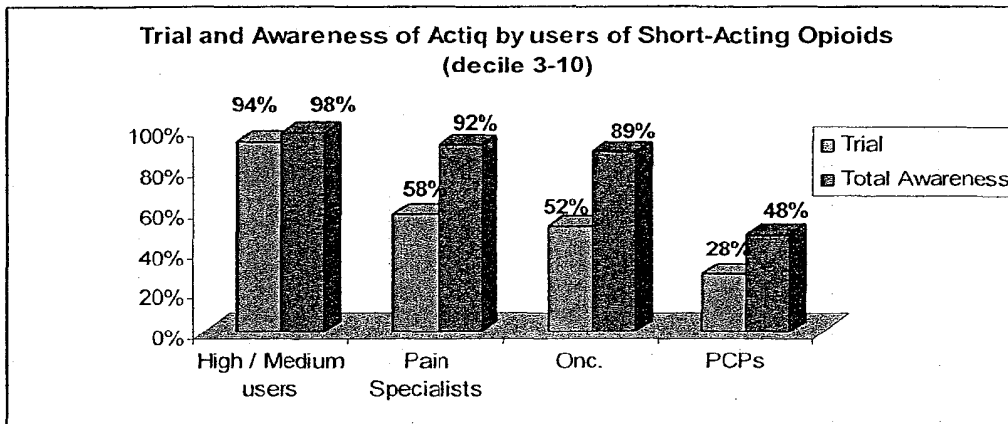
Market research was implemented to assess awareness and trial of ACTIQ among four different segments:

- Medium/high prescribers of ACTIQ (regardless of specialty)
- Pain specialists (both prescribers and non prescribers)
- Oncologists (both prescribers and non prescribers)
- PCPs (both prescribers and non prescribers)

As to be expected, medium/high prescribers regardless of specialty have high awareness (98%) and trial (94%) of ACTIQ. Awareness of ACTIQ among pain specialists and oncologists is similar and fairly high (92%, 89% respectively), but trial of the brand remains low in both segments (58%, 52% respectively). This high awareness is to be expected as promotional efforts have been primarily directed towards these segments



over the last few years. PCP's have both low awareness (48%) and trial (28%). Again, this is to be expected as promotional reach has been limited until the recent expansion of the sales force from 79 to 435 representatives.



Source: Primary research Ziment 03

Trial = ever prescribed

Total Awareness = aided + unaided response

One implication from this research is that couponing should be considered (where allowed) for low user / non-users of ACTIQ that are pain specialists or oncologists to increase trial usage levels. Additionally to complement the expanded reach of the sales force, there is also a need to develop programs for opioid-skilled PCPs that simultaneously increase trial and awareness of the ACTIQ brand and its use for the treatment of BTCP.

### **Perception**

Primary research (Ziment Structure Study, September 2003) was used to identify how current users position ACTIQ. ACTIQ is viewed as:

- a short-acting opioid that provides effective relief as a result of its rapid onset of action for severe pain
- producing typical opioid side-effects
- a unique, easy to use and titrate (method of delivery) medication

The implications of this are that current users accurately reflect the intended positioning, except for the addition of convenience (ease of titration / ease of use) which could enhance the positioning. This is especially important to the opioid-skilled PCP market segment (53% highest unaided advantage).

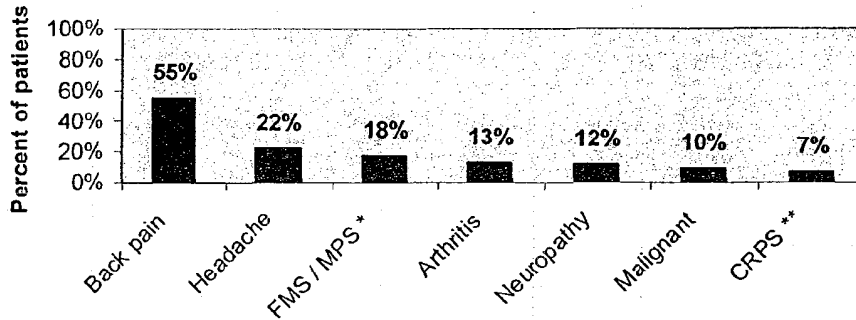
### **Physician Usage**

In order to capture product usage, a validated audit such as The Physician Drug and Diagnosis Audit (PDDA) is used. However, PDDA does not accurately reflect ACTIQ usage due to the lack of anesthesiologists in their sample, which is one of the largest segments and the most productive segment of the ACTIQ prescriber base. Without the ability to use this audit, primary research was conducted. Findings are representative of deciles 3-10 of our total prescribing base. The findings of this primary research are intended to show the proportion of ACTIQ patients that are being treated for each underlying condition.

Based on physician reporting, 90% of ACTIQ use is for BTP outside of cancer, with the majority of use (55% of total) being for chronic back pain. This broad use of ACTIQ suggests there are many prescribers who:

- understand or are experienced prescribing fentanyl
- treat the pain pathophysiology, not the disease state or etiology
- understand the benefits ACTIQ affords their patients
- are comfortable utilizing it beyond its labeled indication

**Distribution of Conditions Treated with ACTIQ  
(Projected)**



Source: IMS Patient Chart Audit, Oct. 2003

\* Fibromyalgia / Myofascial Pain \*\* Complex Regional Pain Syndrome

It should be noted that specialty usage tends to fluctuate based on patient presentation and physician recognition of the need for rapid acting or BTCP/BTP. For example, neurology usage tends to be higher for headache (97%) while PCP usage is higher for back pain (81%).

**ACTIQ Use by Specialty<sup>^</sup>**

	Anes / Pain	Neuro	PCP	Other	Total
Malignant pain	13%	6%	4%	35%	10%
Back pain	49%	21%	81%	41%	55%
Headache	17%	97%	19%	14%	22%
FMS / MPS*	14%	11%	17%	18%	18%
Arthritis	12%	7%	21%	8%	13%
CRPS**	9%	2%	5%	5%	7%
Neuropathy	10%	9%	21%	12%	12%

Source: IMS Patient Chart Audit, Oct. 2003

\* Fibromyalgia / Myofascial Pain \*\* Complex Regional Pain Syndrome

<sup>^</sup>Note: These data will not add to 100% because of multiple uses

It is not surprising that physicians' use of ACTIQ has expanded beyond its indication. The ACTIQ clinical trials conducted studies in various cancer patients with persistent pain syndromes that could be characterized as either nociceptive or neuropathic, with BTCP that was determined to be an extension of their persistent pain. In addition, although the clinical trials were not designed to compare OTFC with other medications used for BTCP, exploratory analysis found that OTFC provided significantly greater analgesic effect at 15, 30 and 60 minutes and a more rapid onset of effect than the usual short acting medications used.

While the ACTIQ trials showed its efficacy and rapid action for BTCP in cancer patient populations, physicians who treat pain most often consider cancer pain no different than non-cancer pain and treat it the same regardless of etiology.

In addition, many physicians are already familiar with fentanyl, so once they recognize the rapid onset of ACTIQ, they determine who the ideal patients for ACTIQ are - those that will benefit from its rapid onset of analgesia. Physicians easily apply the learnings from the ACTIQ trials to their clinical practice and make decisions every day on which medication will best suit that patient to address their needs. Because physicians can use products wherever they deem appropriate, they have expanded ACTIQ's use to a larger patient population.

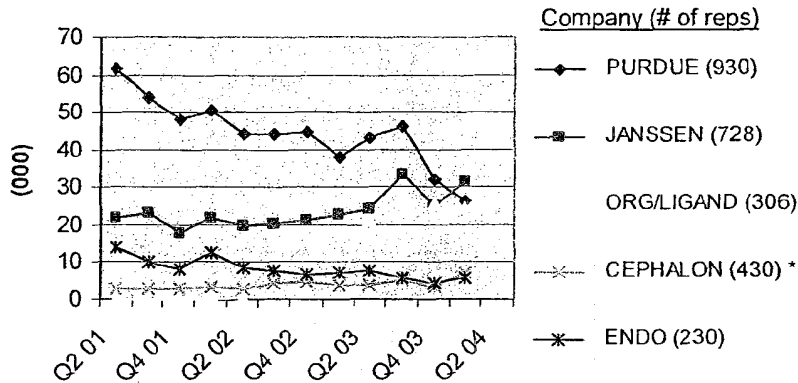
## **F. COMPETITION**

### ***Competitive Environment – Physician Contacts (share of voice)***

The major companies in the pain marketplace currently marketing branded pain medications (i.e., not devices, not generics) include Purdue Pharma, Janssen, Organon / Ligand (partnership) and Endo, with Purdue Pharma and Janssen being the dominant market leaders. These companies have primarily focused on the outpatient chronic pain market for long-acting, sustained release products (although most offer both long and short-acting products).

Purdue's presence has recently declined due to the generic competition of OxyContin but the overall competitive share of voice ACTIQ faces has not decreased significantly because Organon has partnered with Ligand to market Avinza (long-acting morphine). In terms of sales representative activity (based on physician perception) Cephalon has recently surpassed Endo in physician contacts. However, Cephalon continues to face a competitive market with sales forces that are larger and focused solely on the pain market.

**Leading Pain Companies - Physician Contacts**



Source IMS IPS (contacts) and Verispan and Company reports for # of reps  
 \* ACTIQ receives 16% of the primary equivalent details (SMART system)

**Total Opioid Volume in TRxs**

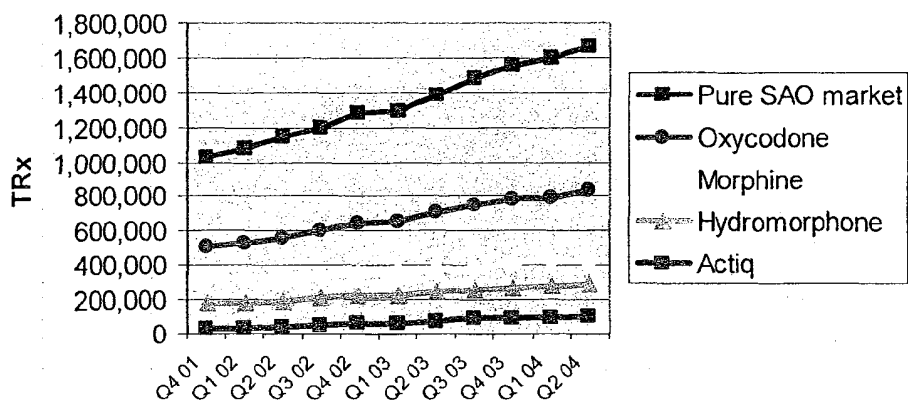
To provide some perspective on the opioid market, a table summarizing the entire opioid prescription market follows:

**MAT July 2004**

Total opioid TRx	166.8 MM
Total 5 combination short acting	133.0 MM
Top 5 long acting	14.4 MM
Top 5 pure short acting	8.0 MM
ACTIQ TRx	404 K
• 5% TRx share of top 5 pure SAOs	

The graph below illustrates the growth of the overall pure SAO market, as well as the three opioid compounds in the class (morphine, oxycodone and hydromorphone) and ACTIQ (fentanyl). The pure SAO TRx market has grown an average of 21% over the last two years (MAT August 2003 and MAT August 2004), with the majority of the growth being contributed by oxycodone.

### Pure SAO Market Growth



#### Pure Short-Acting Opioids – (Direct Competitors)

ACTIQ's direct competitors are the pure SAOs. This marketplace includes both branded and generic products with the generics dominating TRx market share (80% of TRx in MAT Q2 2004). Despite the heavy reliance of the market on oral short-acting pure opioids for the treatment of BTCP, these products generally take 30-45 minutes to work. ACTIQ has a clear and distinct advantage over the currently available products in this category with its more rapid onset.

#### Pure Short-Acting Prescription and Market Share Analysis

Short Acting Opioid Class	TRx Q2 03	MAT %	TRx Q2 04	MAT %	Δ
Oxycodone HCL (G)	1,690,832	31%	2,481,743	38%	47%
Morphine Sulf (G)	1,241,729	23%	1,667,464	26%	34%
Hydromorphone HCL (G)	675,206	12%	885,317	14%	31%
Roxicodone (B)	563,722	10%	507,163	8%	-10%
ACTIQ (B)	247,256	5%	397,151	6%	61%
Dilaudid (3 types) (B)	212,428	4%	184,524	3%	-13%
Roxanol (4 types) (B)	236,472	4%	150,317	2%	-36%
Codeine (G)	102,632	2%	105,941	2%	3%
OXYIR (B)	225,909	4%	75,022	1%	-67%
MSIR (B)	161,733	3%	27,875	0.4%	-83%
OXYFAST (B)	58,853	1%	21,381	0.3%	-64%
<b>Class Total</b>	<b>5,416,772</b>	<b>100%</b>	<b>6,503,898</b>	<b>100%</b>	<b>20%</b>

(G) = Generic

(B) = Branded

All of the generic products showed growth from MAT June 2003 to MAT June 2004, while all of the branded products except ACTIQ had negative growth. ACTIQ

prescriptions have grown 61%, a faster rate than any other pure short-acting product, branded or generic. For this same time period ACTIQ increased its market share from 5% to 6%, while all the other branded products lost market share.

It is important to note that all opioids are operating within the same environment, although each opioid product may have different inherent benefits and risks associated with them. Also, it is important to note that the overall pure short-acting opioid market continues to grow, most recently growing 20% over MAT Q2 2004. Despite the fact that ACTIQ has grown TRx market share since 2001, it maintains a small share of the pure SAO TRx market, providing much opportunity for growth.

***Combination Short-Acting Opioids – (Indirect Competitors)***

As evidenced in primary and secondary market research, opioid combination products are often prescribed for the treatment of BTCP but are less than ideal for the following reasons:

- Limited dosing flexibility due to low opioid dosage options (for use in mild to moderate pain only)
- Dose ceiling effect due to presence of APAP, ASA, and NSAIDs causing intolerable side effects

Physicians are using this class of drugs to treat BTCP, acute pain, chronic pain and episodic pain as a result of their ease of use. These drugs do not require a complicated approval process (e.g. triplicate prescriptions required in some states, CIII allow for phone-in prescriptions and refills) and have greater availability at pharmacies.

***Long-Acting Opioids – (Indirect Competitors)***

Long-acting opioids are most commonly prescribed to treat the persistent pain component of chronic cancer and non-cancer pain in patients who are considered opioid tolerant. Chronic pain is loosely defined as pain that persists for a specified time that is arbitrarily determined (e.g., 3 months or 6 months), or beyond the expected period of healing. The duration of analgesia ranges from 8-72 hours, while onset of analgesia ranges from 45 minutes to 12 hours. The convenience afforded by the duration of analgesia is the key benefit of long-acting opioid products. The onset of analgesia is not a differentiating factor for long-acting opioids. A chart of the long-acting opioids is included as appendix 2.

Long-acting opioids are not considered a direct competitor in the BTCP market. However, they may be viewed as an indirect competitor for ACTIQ. Various manufacturers have aggressively educated physicians to minimize the occurrence of BTCP (i.e., that when appropriately medicated with a long-acting opioid, patients should not experience BTCP). They promote increasing the dose or the frequency of the long-acting medication to avoid BTCP flares. Although not congruent with the opinions of most key opinion leaders, many community-based physicians currently adhere to this philosophy, thus turning the long-acting opioids into “pseudo-competitors.” Again educating physicians will be a challenge.

### ***Competitive Products Summary***

The implications of these indirect and direct competitors are that physicians have varying degrees of education regarding pure short-acting, combination and long-acting opioids. This is an excellent opportunity for Cephalon to help educate physicians about the features and benefits of ACTIQ over direct and indirect competitors when treating BTCP.

### ***Immediate Release Opioids in Development***

The success of the ACTIQ brand has increased competitive clinical development for the treatment of BTCP. It should be noted that several companies are developing immediate release opioids that have the potential to compete with ACTIQ (e.g. Endo, Biovail) in the treatment of BTCP. A comprehensive list (phase II or higher) of potential fast acting opioids is listed as appendix 2.

#### **Immediate release opioids (> phase III)**

<b>Company</b>	<b>Product and / or technology</b>
Endo/Orexo	Rapinyl (tablet – sublingual fentanyl)
Endo/Penwest	Oxymorphone Immediate Release
Alza (JNJ)	Ionsys (E-trans)
Cephalon, Inc.	OraVescent® containing fentanyl
Biovail	Relivia (flash dose of tramadol)

With the recent acquisition of CIMA, the OraVescent® containing fentanyl product (OVF) will provide the market with an additional rapid acting opioid. The OVF product may launch as early as Q4 2006. It will be important not only to prepare for new competitive entrants, but also to prepare the market for the features and benefits OVF will provide.

Please see full list of future competitors in appendix 3.

## **G. REIMBURSEMENT UPDATE**

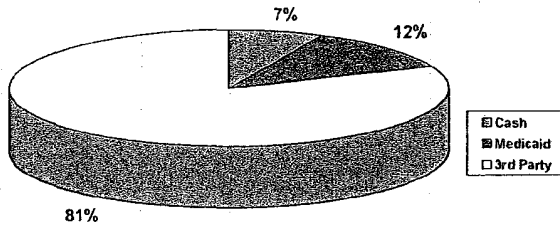
### ***Market Overview***

Securing favorable reimbursement is critical to ACTIQ success and continued growth. ACTIQ has had the luxury of operating under the radar screen within managed care marketplace for a number of years. Though ACTIQ generally continues to experience a favorable reimbursement status, there has been an increase in the implementation of restrictive measures in an attempt to limit access both in the commercial as well as Medicaid segments. These reimbursement hurdles include Prior Authorization, documentation of a BTCP indication, requirements for documented use of formulary agents prior to ACTIQ, and/or quantity limits restrictions. In addition, patients are facing higher co-pays than previously required.

ACTIQ sales can be broken into three payers or segments; patients who pay cash for their prescription, the government (Medicaid), and third party, which includes anyone other than the patient or government paying for a script. This would include managed care,

insurers, worker's comp and employers. The following graph illustrates the breakdown of each segment for ACTIQ calculated by total units for the 2<sup>nd</sup> quarter 2004:

### ACTIQ Payer Segments



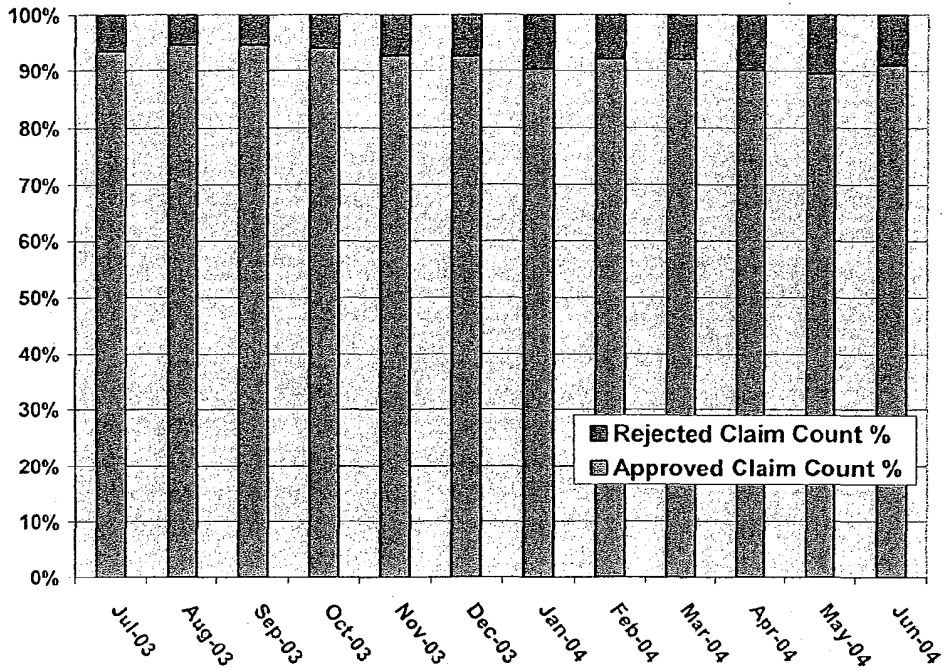
Source: 6/04 NDC Smartplan

#### **Managed Care**

The majority of ACTIQ total business resides in the 3<sup>rd</sup> party segment at a little over 80%. The vast majority of this 80% is made up of managed care organizations or commercial insurers whose business can be further defined into essentially 3 different types; employers, Medicare eligible and Medicaid carve out. As mentioned above these managed care organizations are increasing restrictions on reimbursement. Though the majority of ACTIQ managed care claims continue to be approved (approximately 90% in the first half of 2004) the 2004 monthly percentages are down slightly compared to the last half of 2003 (92%-95%).



### ACTIQ Prescription Claim Status 7/03-6/04



Source: June NDC Dynamic Claims Analyzer

One area of concern that the managed care group monitors closely is the trend toward greater cost sharing through higher copays and coinsurance (% cost of a script). This trend is exemplified with increased patient rejections as copays, and more importantly, as coinsurance increases in specific markets. Though it is a small percentage of the overall pharmacy benefit that is offered by insurers, coinsurance is certainly an area to monitor closely considering Cephalon's premium priced products. The table below provides an overview of the percent breakdown of total approved claims and reversals by copay range as well as the rate of reversals that are attributed to a particular copay range according to Q2 2004 NDC Dynamic Claims Analyzer (DCA).

Q2 2004					
Cost Range	Approved Claim Count	Total Approved Claim % Breakdown	Reversed Claim Count	Total Reversed Claim % Breakdown	Reversed Claim % @ Copay Level
\$0.00	4,999	34.75%	71	9.90%	1.40%
\$0.01 - \$5.00	845	5.87%	11	1.53%	1.29%
\$5.01 - \$10.00	1,197	8.32%	91	12.69%	7.07%
\$10.01 - \$20.00	2,045	14.22%	136	18.97%	6.24%
\$20.01 - \$40.00	3,224	22.41%	215	29.99%	6.25%
\$40.01 +	2,074	14.42%	193	26.92%	8.51%
<b>Total</b>	<b>14,384</b>	<b>100.00%</b>	<b>717</b>	<b>100.00%</b>	<b>4.75%</b>

Source: June NDC Dynamic Claims Analyzer

Additionally, claims data reveal increasing percentage of claim reversals are due to prior authorizations (17.7% second half of 2003 vs. 25.4% first half 2004) and plan limits being exceeded (17.8% second half of 2003 vs. 22.7% first half 2004).

**ACTIQ Claim Rejection Reasons**

ACTIQ Claim Rejection Reason	Q303	Q403	Q104	Q204
PRIOR AUTHORIZATION REQUIRED	15.1%	20.3%	22.7%	28.1%
PLAN LIMITATIONS EXCEEDED	19.1%	16.5%	23.5%	21.9%
COST EXCEEDS MAXIMUM	2.1%	2.2%	1.3%	1.6%
DAYS SUPPLY LIMITATION FOR PRODUCT/SERVICE	0.0%	0.1%	0.1%	0.1%
PRODUCT/SERVICE NOT COVERED	7.1%	7.4%	5.7%	4.5%

Source: June NDC Dynamic Claims Analyzer

Though managed care has, for the most part, been relatively unsuccessful at slowing or stopping ACTIQ, the National Account Management team will continue to focus on securing and maintaining favorable reimbursement status for ACTIQ in order to minimize the negative perceptions or "collateral affect" that the restrictions could have on the prescribing habits of some physicians. Though unquantifiable, the "indirect" impact of these managed care restrictions is the loss of "potential business". The greater the hurdles to prescribing ACTIQ the more likely a physician will be to select an alternative pain medication for his or her patients. Recent market research with ACTIQ prescribers who have decreased or leveled off in their writing showed that declining insurance coverage is most frequently mentioned as the reason why. This same research also asked dabblers – those who have just started writing ACTIQ - to list the barriers to writing more ACTIQ and, despite their admission that it works very well, they see insurance issues as a major hindrance.

**Medicaid**

State Medicaid programs continue to be subjected to state budgetary pressures and therefore are increasingly moving toward preferred drug lists, prior authorization and supplemental rebate programs. ACTIQ has been put under prior authorization in a number of states over the course of the last year with anticipation that that trend will continue. Currently, 16 states have ACTIQ under a prior authorization with truly limited success in denying access to the product. To provide some perspective, in the Medicaid segment, as of Q2 2004, ACTIQ grew 9% versus the previous quarter, while the pure SAO market grew 21%. The majority of states continue to allow unimpeded access, however there is a core set of states that represent the largest portion of sales. Over 50% of all Medicaid ACTIQ units are generated from the top 5 states. The following is a list of these top five states ranked by percent of total Medicaid business based on units: (Source: Q2 2004 NDC Smartplan)

<u>State</u>	<u>% Total Medicaid</u>
California	14.31%
New York	14.14%
New Jersey	8.13%
Florida	7.59%
North Carolina	6.88%

Two states in particular, California and New York comprise close to 30% of the Medicaid business. Interestingly enough, California now has a prior authorization in place and continues to perform well. New York does not have a prior authorization or PDL program in place which currently allows open access to ACTIQ.

Obtaining and maintaining favorable reimbursement status for ACTIQ is expected to be more of a challenge in the coming years. The National Accounts Management Team will continue its efforts in this area. Additionally, the current Reimbursement Hotline is being evaluated to determine ways in which it can be strengthened to better support physicians and patients in seeking reimbursement for ACTIQ.

## H. MEDICAL EDUCATION

### *Continuing Medical Education*

CME played a vital role in the education of physicians, nurses and pharmacists in 2004 regarding chronic cancer pain and non-cancer pain and Abuse, Addiction and Diversion. The major CME initiatives in 2004 included a CME on-demand teleconference, local and regional CME symposia (*CEP Lectures*), a tri-mesterly newsletter entitled *Emerging Solutions in Pain*, a repository website by the same name *EmergingSolutionsinPain.com*, sponsorship of the *Pharmacologic Management of Pain Resource Center* on Medscape and the sponsorship of the Breakthrough Cancer Pain category on *pain.com*, the most popular pain website on the internet. Additional CME initiatives included a CME insert in *CME-TODAY* for Primary Care Physicians and CME Symposia at the annual congresses for AAPM, AAPM&R and the Northeast PRI-MED.

The local and regional CME Symposia represented one of the most significant educational efforts in the area of pain management in 2004. These symposia allowed for the scientific exchange of extensive information on diagnosis, assessment and management of various pain related issues. Approximately 214 of these programs are expected to be completed by year end.

The tri-annual newsletter, *Emerging Solutions in Pain*, currently has a circulation of over 11,000 clinicians (8,000+ physicians and 2000+ nurses). The newsletter allows for communication of information on diagnosis and management of various pain types, in two distinct media: written and CD-ROM. The accompanying website serves as a repository for all CME programs created.

Note that for 2005 the *Emerging Solutions in Pain* name will be used for a different initiative, which will be discussed in detail. If the decision is made to continue support of the website and the tri-mesterly newsletter they will be re-launched under a new name.

## I. PROMOTIONAL ACTIVITIES

### *Promotional Medical Education Programs*

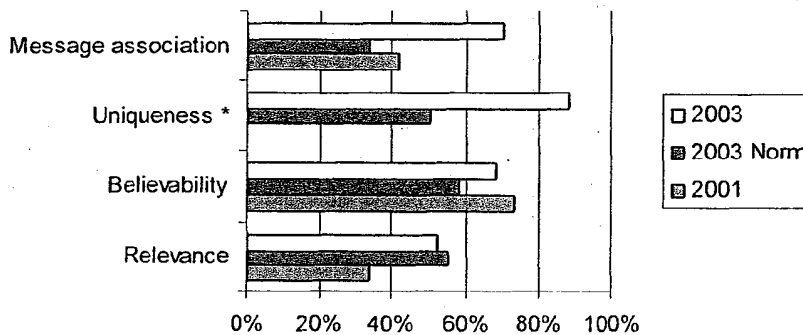
Sales-driven Medical Education Programs (MEPs) are also a critical component of the educational efforts for ACTIQ. In 2004, over 1600 sales-driven MEPs will be executed with greater than 4800 clinicians exposed to ACTIQ promotional messaging.

### *Advertising Campaign*

The concept currently in use for ACTIQ is the "bell" concept which was developed early in 2001. This concept has been utilized in all branded promotional and advertising materials since. Based on market research findings in 2002 the headline was enhanced to say "When Onset Matters...ACTIQ On Call" and the tagline was changed to say "When Onset Matters".

In July 2003, a Campaign Tracking Study (CTS) was initiated with ACNielsenHCI to evaluate the concept's overall effectiveness. More specifically, the study measured physicians' ability to recognize and recall the advertisement as well as the believability, relevance and uniqueness of specific messages within the advertisement. The headline was changed from "ACTIQ on call" to "When onset matters...ACTIQ on call," which contributed to a significant improvement in the ACTIQ ad campaign.

**ACTIQ Campaign Evolution**



\* Uniqueness not tested in 2001

Source: AC Nielson

ACTIQ has also made significant progress in unaided top of mind awareness for Breakthrough Cancer Pain (2% in 2002 vs. 8% in 2003), but has less than half of the awareness of competitors Percocet and OxyContin (18-20% - 2003).

In order to identify additional enhancements to the campaign, a "brand portrait" study was conducted in March 2003 to identify key emotional, attitudinal and relational themes for the optimal emotional positioning of ACTIQ. A secondary objective was to understand physicians' motivations, desires/needs, feelings, satisfactions and frustrations with respect to BTCP and its treatment.

This study found that pain specialist drew the greatest satisfaction from restoring patients' quality of life and daily functioning. Pain specialists are frustrated by patient addiction worries while being disappointed with poor pain control (especially true for BTCP). High users of opioids felt that depicting patients with restored quality of life and improved daily functioning implies power (potency) to relieve BTCP as well address a prime physician motivation in this treatment area.

Based on these market research findings marketing is evolving the ACTIQ campaign to include a more humanistic approach while trying to maintain the brand equity associated with the successful "bell" campaign. The humanistic concepts were tested against the original campaign and were preferred by 77% of the physicians. It is also interesting to note that despite the high marks the current campaign received in the most recent CTS, none of the pain specialists felt the current campaign was the most compelling (Ziment 7/04). The final enhanced concept is currently being tested and an example of the revised campaign is in appendix 4.

## J. MARKET DYNAMICS

### *Pain Market*

Pain is a prevalent medical problem that impairs the quality of life for millions. Pain can be short-lived, it can persist for months, or it can debilitate people for the rest of their lives.

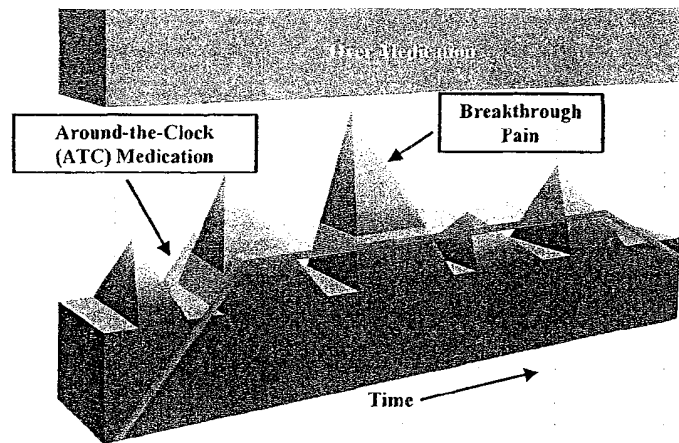
Pain can be classified in three distinct ways. It can be classified by 1) temporal aspects, 2) cancer versus non-cancer and 3) pathophysiology. Physicians consider each of these classifications in selecting an appropriate therapeutic agent(s) for an individual patient.

#### 1) Classifying Pain by Temporal Characteristics:

- Acute pain – pain of a relatively short duration that disappears as healing occurs (e.g., injury or trauma)
- Episodic/recurrent pain – intermittent occurrences of pain, with each episode lasting for a brief period of time but recurring across an extended period of time (e.g., migraine, sickle cell pain crises)
- Chronic pain – pain that persists beyond the time healing is expected to occur

The challenge of managing chronic pain is significant because of physiologic changes that occur as chronic pain develops. Moreover, chronic pain comprises two distinct components – persistent pain and breakthrough pain (BTP) – making it even more difficult to manage.

## Chronic Pain Components: Persistent & Breakthrough Pain



BTP is a transitory flare of pain of moderate-to-severe intensity over ongoing, persistent pain in patients receiving chronic opioid therapy. BTP is a prevalent form of pain in patients with both malignant and nonmalignant diseases. Patients with BTP suffer from both physical consequences (e.g., reduced functional ability and poorer overall health) and psychological consequences (e.g., frustration, fear, anxiety and depression). BTP not only has a negative effect on patients' quality of life, it also increases the economic burden to both patients and the healthcare system.

### 2) Classifying Pain as Cancer vs. Non-Cancer

Pain has traditionally been classified as cancer and non-cancer pain. Classification of pain in this manner is evolving. Historically, practitioners have viewed cancer pain and non-cancer pain as different entities, however, this type of classification is being challenged by pain thought leaders and professional societies. Physicians have begun to shift their thinking from disease state (e.g., cancer vs. non-cancer) to the pathophysiology of pain.

### 3) Classifying Pain by Pathophysiology

Pain can be classified by its pathophysiology as either nociceptive or neuropathic pain. Nociceptive pain originates within normal pain pathways, appears to be proportionate with identifiable tissue damage, and has a fairly predictable response to analgesics. Neuropathic pain is caused by damage to the nervous system, is sustained by aberrant somatosensory processing, and has a less predictable response to analgesics.

### *Opioid Market*

Opioids are the mainstay of treatment for patients suffering from moderate-to-severe acute and chronic pain. The prescription opioid market is divided into two major categories:

1. Long-acting opioids
2. Short-acting opioids

## 1. Long-Acting Opioids

Long-acting opioids are most commonly prescribed to treat the persistent pain component of chronic pain in patients who are considered opioid tolerant. The duration of analgesia ranges from 8-72 hours, while onset of analgesia ranges from 45 minutes to 12 hours.

## 2. Short-Acting Opioids

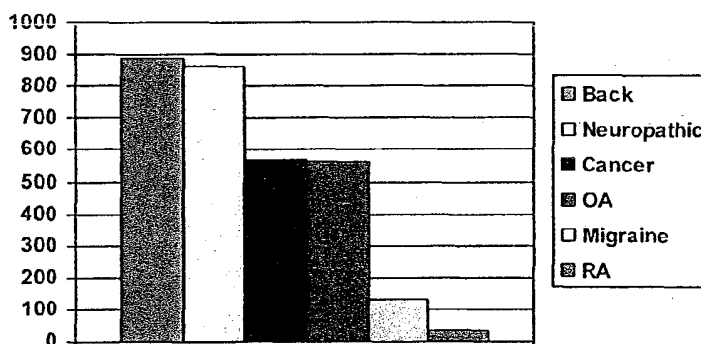
The short-acting opioid market can be further subdivided into two categories:

- Pure short-acting opioids
- Combination short acting opioids (opioid plus NSAID/acetaminophen/aspirin)

Currently, both pure short-acting opioids and combination products are commonly used to treat opioid naïve patients suffering from acute pain and recurrent or episodic pain, as well as opioid tolerant patients suffering from BTP/BTCP. Currently available oral short-acting opioids (tablets and solutions) provide onset of analgesia over a range of 30-60 minutes while the duration of action ranges from 4-6 hours.

The chart below displays the primary chronic pain disease state areas in which short-acting opioids (pure and combination products) are utilized:

**Number of Patients Treated with Opioids by Chronic Pain Type (000)**



Note: Adjusted for co-morbidity, Back Pain only includes moderate-to-severe segment  
Source: Analysis of Secondary Market Research Reports by Cephalon Market Research, 2004

Despite the fact that both pure SAO and combination products are used to treat BTCP/BTP Cephalon considers its primary market for BTCP to be the pure short-acting opioids (SAO).

### ***Breakthrough Cancer Pain Patients***

Breakthrough Cancer Pain patients are treated with both pure short-acting opioids (e.g., OxyIR, MSIR) and combination opioid products (e.g., Vicodin, Percocet). Primary market research performed in 2004 indicates that pain specialists and oncologists prefer to utilize OxyIR and MSIR (pure short-acting opioids) for the treatment of BTCP, while

primary care physicians who are high writers of opioids prefer combination opioids such as Vicodin and Percocet. This research also highlighted the commonness of Percocet, a combination opioid (oxycodone & acetaminophen), as a preferred choice of BTCP medications across all physician specialties of all opioid usage levels (Ziment Pain Medication Structurez Study, February, 2004). ACTIQ had high awareness and utilization among high prescribers of opioids. The implication of this research is that despite having a superior clinical profile, the market has not adopted ACTIQ as a preferred treatment option for BTCP.

### ***Market Challenges***

#### **Evolving Pain Guidelines**

Treatment guidelines have been established for both cancer pain and non-cancer pain over the last several years and continue to evolve. Unfortunately, these published guidelines are limited in their discussion of BTP/BTCP. To date, no treatment guidelines specific to BTP/BTCP have been established.

#### **Abuse, Addiction and Diversion**

Unfortunately, under-treatment of pain continues to be a widespread problem. It has been postulated that one reason why pain is under-treated is due to physician fear of prescribing opioid analgesic medications (opiophobia). This fear is mostly attributed to concerns of abuse, addiction and diversion, as well as scrutiny by regulators that monitor the prescribing and dispensing of these medications. Despite mounting evidence demonstrating that effective analgesia improves quality of life, this fear persists. In general, physicians try to balance fear of opioid abuse (addiction and diversion) and regulatory scrutiny with the patients need for medications that provide safe and effective analgesia while improving daily functioning and restoring quality of life.

Many clinicians have expressed a great need for assistance in the assessment of the risk of abuse, addiction, and diversion among the pain patient population. This is the primary reason Cephalon has committed itself to establishing a comprehensive education and awareness program for risk minimization with the goals of minimizing risk to patients, the public, and physicians themselves. This program is entitled *Emerging Solutions in Pain (ESP)*. *ESP* is an ongoing initiative that is being developed by physicians for physicians, pharmacists and other healthcare professionals, to address some of the most critical issues in pain management today. These issues involve balancing the fundamental rights of patients and clinicians with the challenge of identifying patients who are at greater or lesser risk for opioid misuse and addiction, and with the challenges associated with the complex regulations involved in prescribing controlled substances. Through the expertise of a cadre of leading pain and addiction medicine experts, the *ESP* program will provide clinicians with guidance in the implementation of good practice management techniques, emphasizing favorable interaction with regulatory and law enforcement agencies, as well as, effective assessment, monitoring and documentation strategies, which will contribute to the overall goal of optimizing outcomes for their pain patients. *ESP* is a branded educational initiative owned by Cephalon, Inc in order to support the Risk Minimization Strategy Team (RMST) and the Pain Franchise.



### III. SWOT ANALYSIS AND KEY MARKETING ISSUES

#### A. ACTIQ SWOT ANALYSIS

STRENGTHS	WEAKNESSES
<ul style="list-style-type: none"> <li>• Rapid onset of analgesia</li> <li>• Solid clinical database within cancer pt population</li> <li>• OTC delivery and onset of action provides pts with:               <ul style="list-style-type: none"> <li>◦ Portability</li> <li>◦ Convenience</li> <li>◦ Control</li> </ul> </li> <li>• Studies available on QoL</li> <li>• Core product characteristics appropriate for Tx of BTCP</li> <li>• Strong 5 year history of efficacy and safety data</li> <li>• 1st RMP pre-launch</li> </ul>	<ul style="list-style-type: none"> <li>• Narrow indication</li> <li>• Cannot make the claim "rapid onset" despite the clinical data</li> <li>• Challenging sales process</li> <li>• Patent expiry approaching and FTC mandate with Barr</li> <li>• Limited promotional flexibility due to Subpart-H approval</li> <li>• Perceived cumbersome titration process</li> <li>• No equianalgesic dosing guidelines</li> <li>• High acquisition cost (limited pharmacoeconomic data available)</li> <li>• Perceived safety concerns</li> <li>• New labeling on dental decay</li> </ul>
OPPORTUNITIES	THREATS
<ul style="list-style-type: none"> <li>• KOL eagerness to evaluate and establish standards for BTP Tx</li> <li>• Increased focus on pain management from JCAHO (5<sup>th</sup> vital sign) and NIH (Decade of Pain Control and Research)</li> <li>• Opioid use being recommended and incorporated into a variety of treatment guidelines (APS, DEA consensus statement, etc.)</li> <li>• Increased awareness of BTCP for patients, providers, and payers</li> <li>• Aging population</li> </ul>	<ul style="list-style-type: none"> <li>• Increased reimbursement issues</li> <li>• No treatment guidelines for BTCP</li> <li>• "Opiophobia" within pain market due to continued publicity around abuse, addiction, diversion (a/a/d)</li> <li>• Increased media attention around issues of (a/a/d)</li> <li>• Continuing negative patient and prescriber reaction to compressed powder formulation</li> <li>• Potential negative reaction to sugar free formulation</li> <li>• Difficult promotional development process with FDA review and comment</li> <li>• Increased counter-detailing from competitors</li> <li>• Competitors continuing to be used to treat BTCP without label/indication for BTCP</li> <li>• Dental decay language in PI/PL</li> <li>• Potential future branded competitors: Rapinyl (Endo)</li> </ul>

#### B. KEY MARKETING ISSUES

Eleven marketing issues have been identified and must be addressed in 2005. It is evident based on the situation analysis that the first six of these issues are the primary issues that must be addressed in 2005. The remaining are ongoing issues, many of which have persisted since ACTIQ was launched in 1999.

##### *Primary Key Marketing Issues (6)*

##### **1. Intensive selling process that requires high skill level, focus and frequency**

Selling ACTIQ is often challenging and time intensive due to a variety of factors, including:

1. Different delivery system - a change in the treatment paradigm

2. Perceived cumbersome dosing/titration process with limited resources to educate
  - o dosed in micrograms, most other pain meds are in milligrams
3. Major education involved
  - o clinicians must first recognize and treat BTCP
  - o clinicians must understand fentanyl
  - o clinicians must understand why ACTIQ and its delivery system are a benefit to their patients
  - o clinicians must understand how to dose and titrate (relative potency)
4. Whole office and pharmacy sell
  - o other office personnel (nurses, PAs, NPs) must understand how ACTIQ works and how to educate patients on using ACTIQ
  - o clinicians and office staff must understand and educate patients and caregivers on safe storage and disposal of ACTIQ
  - o pharmacists must be comfortable storing and dispensing ACTIQ
5. CII medication
  - o accompanying external issues (pharmacies must be approved to stock, clinicians must be savvy in patient selection and monitoring for opioid abuse, stigma attached to opioids, etc)

In 2003, with 79 pain care specialists (PCS) the direct promotional reach for ACTIQ was somewhat limited. However, despite this limited reach and a plethora of challenges, the PCS sales force had only ACTIQ to sell, which provided for an opportunity to develop expertise in the pain arena and for tremendous focus in their selling efforts. This focus allowed the sales force to take the time necessary to address the specific challenges in the ACTIQ sales process and ensure success. In the fourth quarter of 2003, Cephalon cross trained all PCS and CNS representatives to prepare for 2004 when every Territory Sales Specialist (TSS) would be responsible for all three Cephalon products. Additionally, the sales force was expanded to a total of 435 representatives. This interruption and change in the sales force structure may have contributed to ACTIQ losing continuity and momentum, resulting in relatively flatter monthly prescriptions during that time period.

By the beginning of 2004, approximately 83% of the sales force was new to Cephalon or new to ACTIQ and the pain care market. The Regional Sales Director team expanded from three to seven, only one of whom was from the PCS sales force. Additionally, of the 45 Area Sales Managers in the newly formed sales force, only seven of them came from the PCS sales force. In effect, we moved from a sales force comfortable in the pain market, accomplished in selling an opioid in an "opiophobic" environment, and accustomed to the challenging selling process of ACTIQ, to a sales force with minimal experience in the pain market and opioids. This lesser pain-experienced sales force also had the difficult task of learning three distinct drugs and markets and balancing time and selling efforts appropriately.

A recent conversation between Senior Management and the Regional Sales Directors garnered several comments in regards to these issues:

- “ACTIQ requires more time, effort, handholding”
- ACTIQ is a “whole office” sell with information needed for nursing staff, pharmacy, etc.
- Even for the former PCS Team, ACTIQ is taking a backseat to Provigil and Gabitril because in this environment, they are easier to sell
- Lack of “quality time” for ACTIQ given other priorities

From January to May 2003, monthly prescriptions grew 21%, and for that same time period in 2004, the growth has only been 7%. As time goes on, the sales force may gain knowledge of the pain market and start to achieve a comfort level and success selling ACTIQ. Current prescription figures do not indicate that the sales force has gained a skill or comfort level to impact and improve the relatively flat growth trend since fourth quarter 2003. ACTIQ marketing must be prepared to assist the sales force in any way to minimize these sales force issues and maximize any opportunities. This includes tailoring ACTIQ messages to the appropriate segments based on the results of the segmentation research currently underway.

**2. The transition to Sugar Free ACTIQ may result in possible negative reaction from patients and prescribers, and possible manufacturing issues**

In July of 2003, ACTIQ changed to a compressed powder formulation, the first three months of which provided tremendous negative responses from both patients and clinicians. This was evidenced by an exponential increase in patient and physician complaint calls into our Professional Services line. From January to June 2003, the average calls per month were 176. The calls for July, August, and September were 528, 1,109, and 876 respectively. An analysis of longitudinal prescription and attrition rate data showed that discontinuations of ACTIQ spiked in August 2003, and outpaced new patient starts for several months post the new formulation launch (Dendrite Longitudinal Research August, 2004). Although more recent data show that the discontinuation rate of ACTIQ may have returned to its normal attrition rate, ACTIQ marketing must be prepared to handle a potentially similar situation with another new formulation when ACTIQ switches to sugar free in June 2005. Learnings from the previous formulation change will be incorporated into the launch plan of the sugar free ACTIQ. Frequent communication with all internal departments, specifically distribution and logistics and manufacturing, will help marketing manage possible inventory issues, manufacturing concerns, and timing of the launch. Lastly, marketing must continue to be aware of possible reactions from patients and prescribers (taste, texture, dissolvability, etc.) and work to minimize disruption to the brand.

**3. Low awareness in the assessment and treatment of BTCP**

Many of our targeted physicians and healthcare providers believe that they are managing chronic pain adequately despite the fact that most pain assessment tools do not include questions or pain scales specific to BTCP. BTCP must become recognized as a critical

component of chronic pain that must be assessed and treated as a distinct and separate entity from persistent pain.

#### **4. Increasing managed care and reimbursement issues**

Marketing has been tracking managed care and reimbursement issues and only recently have they become more than relatively minimal. As ACTIQ sales have grown, there have been increasing attempts to limit access to ACTIQ with tactics such as preferred drug lists, prior authorizations, and supplemental rebate programs. Marketing must work with the National Account Managers (NAMs) to arm them with specific materials geared toward managed care. Initiatives to provide guidelines for treating BTCP, peer reviewed publications, pharmacoeconomic data are also critical.

#### **5. Environmental Issue: Physician fear/concern of prescribing opioids (“Opiophobia”)**

Opioids have only become more widely prescribed for pain in the outpatient setting over the last 10 to 15 years. There are still concerns among clinicians such as abuse, addiction, accidental ingestion and diversion, especially as a result of the Oxycontin abuse issue which surfaced in 2001 and still resonates. Additionally, physicians are being scrutinized by both their peers and government agencies with respect to their practice of pain medicine and in particular their opioid prescribing habits. It is critical in today’s world of pain medicine that physicians understand how, when and where to prescribe opioids safely. These concerns may have specifically resulted in physicians shying away from prescribing ACTIQ in the past as many physicians relate rapid analgesia with rapid onset of euphoria and thus the potential for abuse. As an emerging competitor in the world of pain medicine and to ensure ACTIQ’s continued acceptance as the ideal BTCP treatment, Cephalon must attempt to set itself apart from other companies marketing opioids and assist physicians by providing a mechanism too appropriately and safely prescribe opioids.

#### **6. Limited number of key opinion leaders (KOLs)**

Both marketing and public relations must develop/renew relationships with KOLs in the field of pain management in order for ACTIQ to gain the exposure and support needed to become a first line treatment option for BTCP. Key opinion leaders must be made aware of the key messages and benefits of ACTIQ, and be encouraged to establish pain treatment guidelines which include BTCP. At this time, there are no guidelines specific to BTP/BTCP and it is ignored or rarely mentioned in most pain treatment guidelines.

#### ***Ongoing Key Marketing Issues (4)***

#### **Increased negative media, regulatory, and law enforcement attention around abuse and diversion of opioids and ACTIQ**

In addition to the opiophobic physicians, increased attention by the media and law enforcement, often placing ACTIQ in a negative public spotlight, is a growing concern. Both local and national newspapers, as well as news channels like CNN, have released stories about opioids and ACTIQ. Some specific examples follow:

April 27<sup>th</sup> Harrisburg, Pennsylvania "-- A narcotic painkiller that looks like a lollipop -- designed to speed relief to cancer patients -- is starting to show up in illegal sales with the nickname 'perc-a-pop.'"

May 17<sup>th</sup> The Wall Street Journal "Health experts and insurers have voiced concerns over abuse of the painkiller ACTIQ, a fast-acting prescription medication."

May 24<sup>th</sup> WBBH-TV (NBC) Channel 20 in Fort Myers, Florida "...a cancer drug that resembles a lollipop is catching the attention of children who are now beginning to abuse it. The Lieutenant Governor was in our area today with a warning about this."

May 25<sup>th</sup> The Washington Post "'People who may be leery about putting something up their nose or putting a needle in their arm might not think twice about taking a couple licks off a lollipop,' said Kevin Harley, spokesman for the attorney general of Pennsylvania."

Whether the information reported is accurate or not, Cephalon needs to be proactive and develop strategies to handle this kind of attention.

There has also been increased scrutiny by the FDA on ACTIQ's use and they have expressed concerns with the growing reports of abuse and misuse of the product.

#### **Low product awareness among patients and prescribers**

Many physicians and healthcare providers remain uninformed about ACTIQ and its benefits in treating BTCP. Increasing the awareness of ACTIQ and its key differentiating benefits of rapid onset of analgesia, portability, convenience and control will be critical to continuing the tremendous growth seen with ACTIQ since Cephalon's launch.

#### **Limited clinical data and publications**

At this stage of the lifecycle, it may be most critical to support data and/or publications that further establish BTCP as a clinical entity requiring specific assessment and treatment.

#### **Lifecycle management / Limited patent life**

As of now, patent expiry for ACTIQ is expected to occur in September 2006, with a possible extension to March 2007 with a pediatric exclusivity approval. The goals are to maximize ACTIQ sales until patent expiry with focused sales efforts to specific targets and to ensure that any efforts towards establishing BTP can also be leveraged for OVF.

#### IV. PRODUCT VISION AND POSITIONING

##### A. PRODUCT VISION

*Vision:* ACTIQ is the ideal first-line option to treat BTCP in opioid tolerant cancer patients.

Although ACTIQ has a limited patent life, there is still opportunity for growth in the BTCP market. ACTIQ must continue to establish itself as a valid first-line treatment option for BTCP in opioid tolerant cancer patients. To achieve this, we must educate the pain community about the importance of assessing and treating BTCP independently from persistent pain, and we must show the benefits of using ACTIQ for BTCP. Additionally, we must educate about the appropriate and safe use of opioids and ACTIQ to reduce opiophobia in the pain community.

##### B. ACTIQ 2005 POSITIONING

ACTIQ's positioning will continue to focus on its key differentiating feature and benefit.

- Key Feature: ACTIQ utilizes a unique oral transmucosal delivery system (OTS™) for rapid absorption of fentanyl
- Primary Patient Benefit: ACTIQ's oral transmucosal delivery system provides the most rapid onset of action among all non-invasive, shorter acting opioids, ideal for BTCP or rapid onset pain

***ACTIQ 2005 Positioning Statement:***

The 2005 positioning statement for ACTIQ reflects the above key differentiating feature and benefit and, as it should at this point in its lifecycle (no changes in label/indication or in the competitive set), is identical to the positioning statement in use since 2003. The 2003 positioning statement for ACTIQ was created to be simple and direct. It informs what ACTIQ is and distinguishes it from its competitors based on its key differentiating benefit.

**ACTIQ is fentanyl in a unique oral transmucosal delivery system that provides the most rapid onset of analgesia of any non-invasive opioid formulation available which makes it the ideal agent for BTP or rapid onset pain, such as BTCP.**

##### C. PATIENT PROFILE

ACTIQ is indicated and promoted for the management of breakthrough cancer pain in patients who are already receiving and who are tolerant to opioid therapy for their persistent cancer pain. ACTIQ is ideal for patients who suffer from sudden onset/rapid offset pain, who desire personal pain control.

V. **MARKETING AND PROMOTIONAL STRATEGY**

A. **2005 OBJECTIVES**

*Marketing Objectives*

The 2005 ACTIQ marketing plan will seek to address all of the issues facing the brand and achieve the following goals:

- Provide the sales force with effective tools as well as providing them with optimal messages for key targets
- Ensure a smooth transition to the sugar free ACTIQ formulation (no disruption in sales)
- Increase awareness of ACTIQ and BTCP among targeted physician specialties/segments and patient populations with specific focus on the physicians in high SAO and LAO deciles
- Further segment the AB targets to identify the highest potential for ACTIQ use
- Identify the specific message platforms directed to various segments to strategically increase prescriber base and drive more rapid productivity
- Continue to develop relationships with KOLs in pain management
- Develop a tool(s) to assist with managed care/Medicaid reimbursement

*Sales and Prescription Volume Objectives*

Factory sales and prescription volume objectives for 2005 are as follows.

2005	Gross Shipments	Demand Sales	TRx
<b>2005 TOTAL</b>	<b>\$ 450.0 MM</b>	<b>\$ 446.3 MM</b>	<b>668K</b>

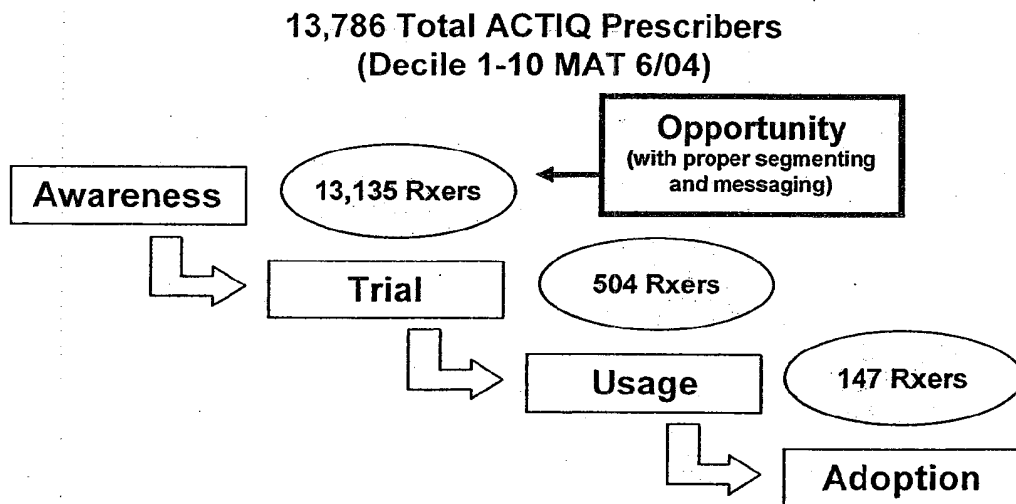
The launch of the sugar free formulation of ACTIQ is expected to occur as early as June 2005. Assuming approval in March 2005, production will start on sugar free ACTIQ to build several months worth of inventory, while at the same time depleting the inventory of sugar-based ACTIQ. Since the strategy is to switch all current patients to the sugar free formulation, there should be minimal disruption to ACTIQ sales and prescriptions. The objectives set forth for 2005 will not be altered to accommodate for the launch since it is a product switch, therefore there are no separate objectives for the sugar free formulation.

## B. MARKETING STRATEGY

### *Overall Promotional Strategy*

As stated above, one of the key objectives for 2005 will be to drive physicians along the product adoption curve from awareness and trial to usage and adoption. Therefore, the overall marketing strategy for 2005 will continue to build on the successful platform developed in previous years, which will be to 1) raise awareness of BTCP and ACTIQ through PR and marketing driven awareness initiatives and 2) differentiate ACTIQ from its competitors by educating clinicians about the core product benefits (rapid onset of analgesia, portability, convenience and patient controlled administration) through targeted medical education initiatives.

When looking at the product adoption curve, 13,135 (95%) of the 13,786 total ACTIQ prescribers fall into the "trial" range. These 13,135 prescribers comprise ACTIQ TRx prescribing deciles 1-4 and represent a tremendous opportunity to grow ACTIQ prescriptions. Only 651 (5%) prescribers fall within the "usage" and "adoption" range of the adoption curve. The 504 "users" comprise the ACTIQ TRx prescribing deciles 5-7 and the 147 "adopters" comprise deciles 8-10. The overall promotional strategy for 2005 will be to continue to move prescribers from awareness and trial to usage and from usage to adoption. Using the results of the segmentation study, there will likely be a way to focus on a subset of the 13,135 trialers to determine who has higher potential and what message should be delivered to them.



A comparison of this information to the previous MAT shows that 42 physicians have moved into the adopter category and 143 more have become users (40% growth for both). Of note is that 3,859 physicians have since trialed ACTIQ, representing increased opportunity to move them into usage and adoption of ACTIQ.



**Prescriber Counts by Decile**

<b>Product Adoption Curve Stages</b>	<b>Prescriber Count MAT Jun 2003</b>	<b>% of total Rxers</b>	<b>Prescriber Count MAT Jun 2004</b>	<b>% of total Rxers</b>	<b>Growth</b>
Adoption (Deciles 8-10)	105	1.1%	147	1.1%	40%
Usage (Deciles 5-7)	361	3.7%	504	3.7%	40%
Trial & Awareness (Deciles 1-4)	9,276	95.2%	13,135	95.3%	42%
<b>Total</b>	<b>9,742</b>	<b>100.0%</b>	<b>13,786</b>	<b>100.0%</b>	<b>42%</b>

*Specific Key Marketing Issues and Strategies*

**Issue: Intense selling process that requires high skill level, focus and call frequency**  
**Strategy: Providing the sales force with effective tools as well as providing them with optimal messages for key sales targets**

The combination of the former CNS and PCS sales forces, followed by the expansion of the sales force, resulted in approximately 83% of the field being new to ACTIQ/pain and new to the ACTIQ marketing team. In addition to the efforts of the sales training department, the ACTIQ brand team must be sure to make the field aware of all educational efforts targeted toward clinicians and encourage them to utilize this information for their own learning. This may help increase their comfort level in the pain market and reduce fear of discussing opioids and ACTIQ. Also, effective tools must be provided to help them overcome barriers and move physicians through product adoption curve. Furthermore, in mid-2004 ACTIQ targets were redefined. Combination products became less of a focus and Duragesic writers were weighted slightly more heavily. Market research is currently underway to further segment target to determine the optimal messages for each segment. Lastly, as always, it will be critical to listen to the field and provide them with appropriate tools and guidance.

**Issue: The transition to Sugar Free ACTIQ may result in possible negative reaction from patients and prescribers, and possible manufacturing issues**

**Strategy: Utilize all learnings from the negative reaction to the compressed powder formulation changeover in 2003 to ensure a smooth transition to maximize the opportunity of sugar free ACTIQ**

More extensive pre-launch market research has been conducted in order to assess reaction to the new taste, texture and dissolvability of the sugar free formulation. This will help us prepare our messages and our launch materials to respond to or possibly avoid negative reaction. Marketing must also be conscious that there may be lingering negativity from the previous formulation change resulting in resistance to another change, therefore some market conditioning with positive messages must get out prior to launch. In order to minimize any hiccups to ACTIQ sales, marketing will create and execute a thorough launch plan and will involve all relevant internal departments to ensure open communication to react quickly, should timelines change, or inventory and

manufacturing issues arise. The launch plan will also map out how we plan to communicate the change to sugar free to all of our audiences, both internal and external.

**Issue: Low awareness in the assessment and treatment BTCP**

**Strategy: Educate key targeted physician specialties and patient populations about the importance of assessing BTCP and the benefits of treating it with ACTIQ**

Through promotional, educational and public relations efforts, marketing will strive to increase awareness of BTCP amongst targeted physicians and patient types. Based on proven success, peer-to-peer promotional efforts and CME will be the primary means used to educate physicians, pharmacists and nurses. PR efforts will be the primary method of reaching and educating patients. In addition, an enhanced convention presence with a large ACTIQ-dedicated booth and an enhanced media presence will be continuing in 2005.

**Issue: Managed Care/Reimbursement Issues**

**Strategy: Address restrictive access to ACTIQ by Managed Care Organizations (MCOs)**

Although 90% of claims are currently being approved, the majority of the market (both commercial and Medicaid) classify ACTIQ as a non-formulary reimbursed drug which has led to a higher co-pay status, prior authorizations (PA) and per diem limits (PDLs). Currently 16 states have incorporated a PA for ACTIQ. California and New York account for approximately 30% of all Medicaid business nationally and California now has a PA in place. The ACTIQ Prior Authorization criteria are:

- Approved within indication and requiring clinical data for uses outside of BTCP
- One or two documented formulary agents used first
- Quantity limits

Also, many providers are limiting access to the opioid class in an attempt to reduce abuse and diversion.

It is very important to address these issues aggressively, as they will not only affect ACTIQ, but may also affect the OVF product. Therefore, marketing has plans for specific managed care initiatives such as publishing and distributing BTP guidelines and disseminating the managed care dossier that should be completed by Q4 2004.

**Issue: Physician fear/concern of prescribing opioids (“Opiophobia”)**

**Strategy: Provide a mechanism to facilitate physician needs for appropriate and safe opioid prescribing habits**

Many clinicians who medically manage pain with opioids have concerns such as abuse, addiction, diversion and accidental ingestion by children. Additionally, scrutiny of opioid prescribing practices by government agencies exacerbate this fear and may affect the opioid prescribing habits of some physicians. As stated previously, these concerns may have specifically resulted in physicians avoiding prescribing ACTIQ, especially since many physicians relate rapid analgesia with rapid onset of euphoria and thus the potential for abuse. Based on the feedback from consultants meetings and advisory panels, Cephalon must attempt to assist physicians by providing a mechanism to prescribe opioids appropriately and safely as well as assess and monitor patients for the

risk of abuse and addiction. ACTIQ marketing has determined that a branded promotional effort/program be implemented as early as Q4 2004 with these specific goals in mind. The objectives and tactics of *ESP* include enhancing clinical practice through ad boards, cases, roundtables, etc; facilitating relationships with physicians, nurses, pharmacists; increasing pain awareness through guidelines, BTP registries, PR, CE, etc; and teaching about balance of opioid use versus risk of diversion by dissemination of the *ESP* toolkit, RMST, roundtables, etc. More detailed tactics of this program are included in the tactics section.

**Issue: Limited number of KOLs**

**Strategy: Build/renew relationships with KOLs in pain management through advisory boards and addition of Scientific Communications Managers**

In 2004, marketing worked with Cogenix to develop an influence map and database of opinion leaders (called IM2) in the pain market. Great strides were made to utilize this influence map to identify, develop and renew relationships with KOLs in 2004. With limited marketing personnel (4 member ACTIQ team) and no field-based support (no medical science liaisons and MDMs not charged with this responsibility), developing relationships with KOLs remains a major challenge and thus a key marketing issue for ACTIQ.

Again, marketing and public relations will initiate/renew contact with KOLs with the objective of receiving guidance in the development of educational initiatives, clinical trials and publication efforts. Also, with the addition of Scientific Communications Managers (i.e., SCM is Cephalon equivalent to medical science liaisons), development of KOLs should be vastly improved in 2005. Marketing will work closely with the SCMs to establish priorities and strategies.

**Issue: Increased negative media, regulatory, and law enforcement attention around abuse and diversion of opioids and ACTIQ**

**Strategy: Establish proactive and reactive strategy and tactical responses to the media and open dialogue with regulatory and law enforcement agencies**

The ACTIQ marketing team continues to work closely with Cephalon Corporate Communications and within the Risk Minimization Strategy Team (RMST) to develop mechanisms to both proactively plan responses and react to any media or law enforcement attention. Additionally, marketing is committed to providing timely and accurate communication of facts to the Cephalon sales force. The goal is for a representative to never be caught off-guard in a physician's office and have the facts necessary to answer any questions that might arise about ACTIQ. Sales management and sales training have been involved in the development of this communication process and are in agreement with its principles.

Cephalon has also opened dialogues with several different groups, including law enforcement. Cephalon executives have met with state attorneys general, as well as the FDA. In July 2004, a group of Cephalon employees met with the FDA to review the current ACTIQ safety record and discuss their concerns. Cephalon is committed to establishing and maintaining a working relationship with the FDA and is dedicated to risk

minimization. Lastly, marketing and other departments plan to meet with DDMAC officials in late 2004 to discuss improving communication and ensure appropriate and on-label promotion of ACTIQ through sales materials.

**Issue: Low product awareness among patients and prescribers**

**Strategy: Strengthen the association of ACTIQ and its key patient benefits through improved awareness and medical education**

The current campaign for ACTIQ – the bell concept – has been used on detail pieces, convention booth panels, and in journal ads (with slight modifications) since 2001. Market research on the campaign has consistently shown that it is effective in conveying ACTIQ's key differentiating benefits. The research continues to show that those who are aware of ACTIQ understand and recall the messages present in the campaign and find them believable, relevant, and unique. ACTIQ has also made progress in top of mind awareness, but overall awareness is still low. In summary, those who are aware of ACTIQ understand and believe the campaign messages; however, overall awareness remains low relative to our target audience and to other pain products. Further market research was conducted and has shown that physicians often choose pain management for emotional reasons, and for the great satisfaction they receive interacting with and treating patients. Because of these 'humanistic' reasons, we are currently in the process of evolving the bell concept to make it more 'human' to appeal to physicians treating pain. The goal is to continue to utilize the bell so as not to lose any of the currently established equity, while adding a human element. ACTIQ's key messages, along with the evolved brand concept will continue to play a critical role in raising awareness of ACTIQ. Market research is currently underway to finalize our evolved concept and the brand team will look to launch the new concept on all promotional materials at the national sales meeting in March 2005.

Additionally, marketing and public relations will implement very specific targeted promotional and educational efforts to continue to raise awareness of ACTIQ among potential prescribers and patients. Also, marketing will be increasing convention activity to help raise awareness. In order to maintain our growth, awareness of ACTIQ associated with its primary patient benefit of rapid analgesia must be enhanced.

**Issue: Limited clinical data and publications**

**Strategy: Support strategic decision making regarding Cephalon-sponsored and IIS research and publication efforts**

At this stage of the lifecycle, it may be most critical to support data and/or publications that further establish BTCP as a clinical entity requiring specific assessment and treatment.

**Issue: Lifecycle management / Limited patent life**

**Strategy: Maximize ACTIQ sales and leverage any opportunities to establish BTP to support OVF**

It is very important to maximize ACTIQ sales through focused sales and marketing efforts on core segments within AB targets and to ensure that marketing driven efforts aimed at establishing BTP can also be leveraged for OVF.

### C. CRITICAL SUCCESS FACTORS

There are 6 critical success factors (CSFs) that must be addressed in order for ACTIQ business objectives to be achieved.

- **CSF #1-** Sales Force is motivated, provided with effective tools and given clear direction on market segmentation and messaging

A motivated and focused sales force is critical for the success of ACTIQ. This is due to both the specialized knowledge of the pain market necessary, as well as the intensive and time consuming selling process. Marketing must improve quality and frequency of interaction with sales force to keep ACTIQ top of mind with the sales force. Marketing must also educate TSS on appropriate messages utilizing the segmentation research results.

Marketing Objectives for CSF #1:

1. At NSM, sales force provided with new materials with evolved concept
2. At NSM, sales force provided with segmented targets and appropriate messages to deliver to those targets (those segments will be tracked to determine PDEs and prescriber productivity)
3. 50% of key targets (based on segmentation research) will receive identified key messages via direct selling or marketing driven promotional efforts by year end

- **CSF #2-** Smooth transition to ACTIQ Sugar Free Formulation (anticipated July 1, 2005)

A key to continued success for ACTIQ will be a smooth conversion to ACTIQ Sugar Free formulation with a minimal disruption in sales momentum. It will be important to communicate and coordinate activities with many internal and external groups to make a timely and seamless transition. In addition, clear communications must take place with the sales force and multiple customer groups (physicians, pharmacists, etc.) to keep them abreast of changes to formulation.

Marketing Objectives for CSF #2:

1. By 3 months pre-launch sales force provided with training and tools to prepare the market for launch
2. At launch, sales force has all necessary promotional materials
3. By 3 months post-launch, prescriber and patient dissatisfaction rate is low - <10% increase in calls to professional services

4. By 3 months post-launch discontinuation rate back to pre-reformulation levels (taking into account brand growth)
- CSF #3- Targeted physicians are aware of both proper assessment and treatment of BTCP and use of ACTIQ

Targeted physicians must have the necessary education and tools in order to recognize, assess and treat BTCP. Cephalon must provide these tools where possible as well as make every effort to provide appropriate educational programs around BTCP.

Marketing Objectives for CSF #3:

1. By end 2005, 29,000 BTP assessment tools disseminated to tier A and B targets by sales force
  2. By June 2005, all ACTIQ prescribers and clinicians (Nurses, PAs, NPs) exposed to the BTP assessment tool/poster via direct mailers
  3. By June 2005, all ACTIQ prescribers and clinicians exposed to the BTP patient brochure via direct mailers
  4. By end 2005, at least 6000 clinicians attend TSS driven MEPs
  5. By end 2005, 40% of target physicians participate in CME programs
  6. By 3 months post publication of the Portenoy BTP survey, disseminate via WLF
  7. By 3 months post publication of the BTP treatment guidelines, disseminate via WLF
  8. By February 2005, establish the comprehensive ISCP (Integrated Strategic Communication Plan)
- CSF #4- Targeted physicians have access to effective tools to allow for optimal reimbursement for ACTIQ

Access to ACTIQ must be maintained. Restrictive formulary status and prior authorization requirements by MCOs must be addressed to ensure that ACTIQ is reimbursed when a physician writes a prescription.

Marketing Objectives for CSF #4:

1. By 3 months post publication of the Portenoy BTP survey, disseminate via WLF
2. By 3 months post publication of the BTP treatment guidelines, disseminate via WLF
3. By January 2005, MCO Dossier distributed to all NAMs and MCOs, and speaker slides completed and a select group of speakers trained on MCO Dossier
4. By June 2005 expand ACTIQ reimbursement hotline and create new reimbursement detail aid
5. By February 2005, establish the comprehensive ISCP (Integrated Strategic Communication Plan)

- **CSF #5-** Targeted physicians are more educated and comfortable about the proper use of ACTIQ and other opioids in their practices.

Physicians have legitimate concerns about abuse, diversion, and addiction when prescribing opioids. In addition, regulatory and legal scrutiny of physician's use of opioids has increased tremendously. Cephalon must address these specific issues and assist in educating physicians in the appropriate prescribing of opioids

**Marketing Objectives for CSF #5:**

1. By 3 months post publication of the Portenoy BTP survey, disseminate via WLF
2. By 3 months post publication of the BTP treatment guidelines, disseminate via WLF
3. By February 2005, establish the comprehensive ISCP (Integrated Strategic Communication Plan)
4. By end 2005, at least 6000 clinicians attend TSS driven MEPS
5. By end 2005, 40% of physicians on target list participate in CME programs
6. By end 2005, at least 10% of physicians on target list sent an e-detail (specifically no-see and hard to reach physicians)
7. By March 2005, ESP website launched and physician target list notified via direct mail
8. By end 2005, 500 ESP Toolkits disseminated to our Tier A targeted list of prescribers
9. By 3 months post ESP-launch 5 cities established as RESPECT meeting sites
10. By end 2005, 3 publications available to the medical community

- **CSF #6-** Key opinion leaders utilize their sphere of influence within the medical community to raise awareness of the need to treat BTCP

The continued development and renewal of relationships with KOLs will be critical to the success of ACTIQ. They must be made aware of the key messages and benefits of ACTIQ and be encouraged to incorporate ACTIQ as part of pain treatment guidelines. Current pain treatment guidelines should also be expanded to include the concept of BTCP.

**Marketing Objectives for CSF #6:**

1. By end 2005, one-on-one interaction with marketing completed with 50% of the top national KOLs (as identified in IM2)
2. By end 2005, 50% of regional KOLs support BTCP guidelines and support ACTIQ as an effective treatment option
3. By end 2005, 50% of local KOLs support BTCP guidelines and support ACTIQ as an effective treatment option

## VI. TACTICAL PLAN

### A. ACTIQ KEY MESSAGES

Before the concept evolution was finalized, message testing was updated in summer 2004 to determine the key messages that most effectively convey ACTIQ's key differentiating benefits and appropriately position the product. ACTIQ will continue to be positioned in 2005 as fentanyl in a unique oral transmucosal delivery system that provides the most rapid onset of analgesia of any non-invasive opioid formulation available through the communication of the following key product messages, which tested highest amongst physicians in summer 2004:

- **Efficacy:** Within 15 minutes of starting medication, patients using ACTIQ rated their pain relief at 67% compared to 3% with their regular rescue medication
- **Safety:** No pharmacologically active metabolites
- **Side Effects:** The most common side effects observed were somnolence, nausea, vomiting, and dizziness
- **Dosing and Titration:** To achieve maximum relief, patients should finish the ACTIQ unit completely in 15 minutes
- **Convenience/Ease of Use:** Patients can use ACTIQ anywhere without water as soon as they begin to feel breakthrough cancer pain
- **Delivery System:** The unique OT delivery system, allows fentanyl to rapidly dissolve into the highly permeable and well-vascularized oral mucosa
- **MOA of Fentanyl:** High lipophilicity of oral transmucosal fentanyl allows for rapid absorption across the oral mucosa into the blood and distribution into the CNS – a process with a 3-5 minute half-life

Some new messages were added based on a review of the clinical study reports. Most of these key messages appear in some fashion in promotional materials, including the most recent journal advertisement (see appendix 5), sales aids and booth panels. All these messages seek to drive home the core patient benefits of ACTIQ.

Following is a table with key messages and allowable claims for those messages:



Key Scientific Message	Allowable Promotional Claim
<b>ACTIQ</b>	
Rapid onset of pain relief	<ul style="list-style-type: none"> <li>• With ACTIQ, pain relief may be observed in 15 minutes. Patients may experience relief while taking ACTIQ, but full relief may not be experienced for up to 45 minutes after finishing an ACTIQ unit</li> <li>• ACTIQ – The only fentanyl product that allows for rapid absorption across the oral mucosa with slower absorption from the GI tract</li> <li>• Analgesic effects of fentanyl are related to blood level, with delay into and out of the CNS – a process with a 3 to 5 minute half-life</li> </ul>
Duration appropriate for BTCP episode	<ul style="list-style-type: none"> <li>• Median time to maximum plasma concentration (<math>T_{max}</math>) across 4 doses of ACTIQ varies from 20-40 minutes as measured after the start of administration</li> <li>• Duration of pain relief was found to be 1 hour (the last time measured) following completion of the ACTIQ unit</li> <li>• BTCP has a median duration of 30 minutes</li> </ul>
Offers convenience	<ul style="list-style-type: none"> <li>• Portability, experience and convenience</li> <li>• Patients can use ACTIQ anywhere as soon as they begin to feel breakthrough cancer pain</li> <li>• Packaged in individual child-resistant blister packs</li> </ul>
Easy to use	<ul style="list-style-type: none"> <li>• Cut...Consume...Clock</li> <li>• The handle has a large "barrel" shape to allow for ease of application and dissolution</li> </ul>
Typical opioid side effect profile	<ul style="list-style-type: none"> <li>• Most common side effects observed in ACTIQ clinical trials were somnolence, nausea, vomiting, and dizziness</li> <li>• The adverse events seen with ACTIQ are typical opioid side effects, and include somnolence, nausea, vomiting, and dizziness</li> <li>• Frequently adverse events will cease or decrease in intensity with continued use of ACTIQ, as the patient is titrated to the proper dose</li> <li>• No pharmacologically active metabolites</li> <li>• The most serious adverse events associated with all opioids are respiratory depression (potentially leading to apnea or respiratory arrest), circulatory depression, hypotension, and shock. All patients should be followed for symptoms of respiratory depression</li> </ul>
Fentanyl – highly lipophilic and no active metabolites	<ul style="list-style-type: none"> <li>• Highly lipophilic for rapid absorption across the oral mucosa with slower absorption from the GI tract</li> <li>• Rapid distribution into the CNS – a process with a 3- to 5-minute half-life</li> <li>• No pharmacologically active metabolites</li> </ul>
OTS™ delivery system ideal for fentanyl delivery	<ul style="list-style-type: none"> <li>• Patented oral transmucosal system (OTS™)</li> <li>• ACTIQ utilizes a patented oral transmucosal system (OTS™) designed for delivery of fentanyl</li> <li>• The unique oral transmucosal delivery system (OTS™) allows fentanyl to rapidly dissolve into the highly permeable and well-vascularized oral mucosa</li> <li>• The ACTIQ matrix dissolves rapidly: 62% in 5 minutes, 93% in 10 minutes</li> <li>• 50% bioavailability of total dose: 25% rapid oral mucosal absorption, 25% slow GI absorption</li> </ul>

General Efficacy	<ul style="list-style-type: none"> <li>Fentanyl plasma levels increase in a dose-dependent manner that is approximately proportional to the dose of ACTIQ administered</li> <li>The analgesic effects of fentanyl are related to the blood level of the drug, if proper allowance is made for the delay into and out of the CNS (a process with a 3- to 5-minute half-life)</li> <li>ACTIQ produced significantly (<math>P &lt; 0.0001</math>) more pain relief compared with placebo at 15, 30, 45, and 60 minutes as measured after the start of administration</li> <li>Efficacy demonstrated in opioid tolerant cancer patients receiving both long-acting oral and transdermal opioids</li> </ul>
Dosing and Titrating	<ul style="list-style-type: none"> <li>75% of patients found a successful dose of ACTIQ</li> <li>Regardless of pain pathophysiology, patients titrated to the same mean dose of 600 mcg</li> <li>Patients started on 200 mcg titrated to a mean maintenance dose of 789 mcg</li> <li>86% of patients were titrated to 400 mcg or higher</li> </ul>
<b>Breakthrough Cancer Pain (BTCP)</b>	
Highly prevalent	<ul style="list-style-type: none"> <li>64% of cancer patients receiving chronic opioid therapy for cancer pain experienced BTCP in spite of controlled persistent pain (N=63)</li> <li>Occurs as many as 4 times per day in many patients</li> </ul>
Often strikes quickly – without notice	<ul style="list-style-type: none"> <li>Breakthrough cancer pain – BTCP – is a transitory flare of pain in patients otherwise controlled with chronic opioid therapy</li> <li>BTCP strikes quickly and without warning in many cases</li> <li>Escalates to maximum severity in many patients in as little as 3 minutes</li> <li>3 categories: spontaneous, end of dose failure, and incident related</li> </ul>
Often subsides within 30 minutes to 1 hour	<ul style="list-style-type: none"> <li>BTCP has a median duration of 30 minutes</li> </ul>

## B. TARGET AUDIENCE

The ACTIQ target audience includes oncologists, pain specialists and physicians skilled in the use of opioids with the potential to treat breakthrough cancer pain. The targeting methodology was updated several times in 2004 and is an ongoing process to ensure that ACTIQ is only promoted to physicians who treat the appropriate patient population.

## C. CORE TACTICAL PLAN

### *Overall Tactical Approach*

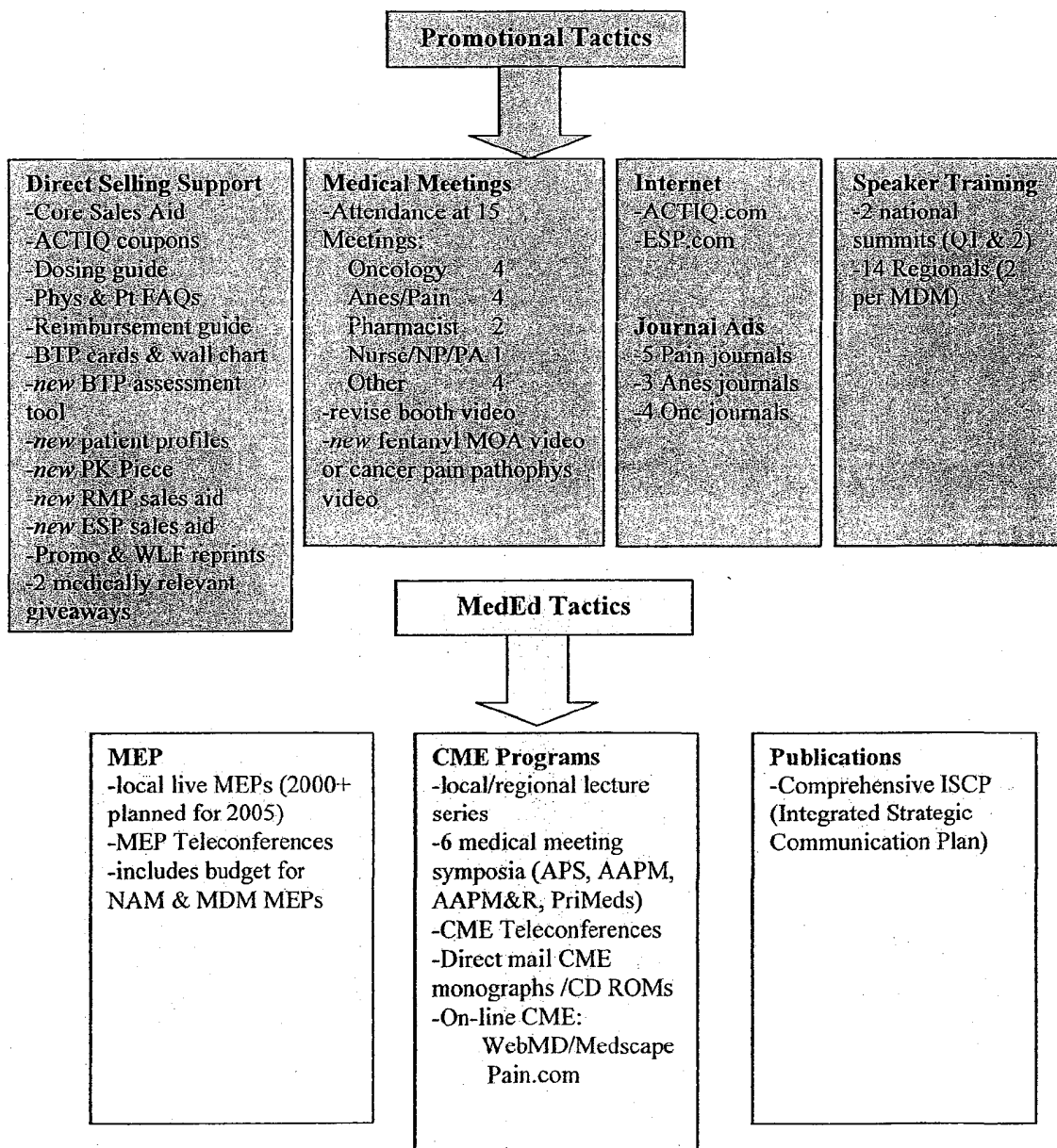
The majority of marketing resources will be allocated to tactics that are considered 1) most effective in delivering ACTIQ's key messages to our target audiences and 2) most effective in educating and raising awareness of ACTIQ and the clinical entity of BTCP. As in 2004, consultant meetings and advisory boards will be implemented to help identify the most appropriate and effective tactical programs to better develop ACTIQ both

commercially and clinically. Therefore, the 2005 ACTIQ tactical initiatives can be broken down into four broad categories:

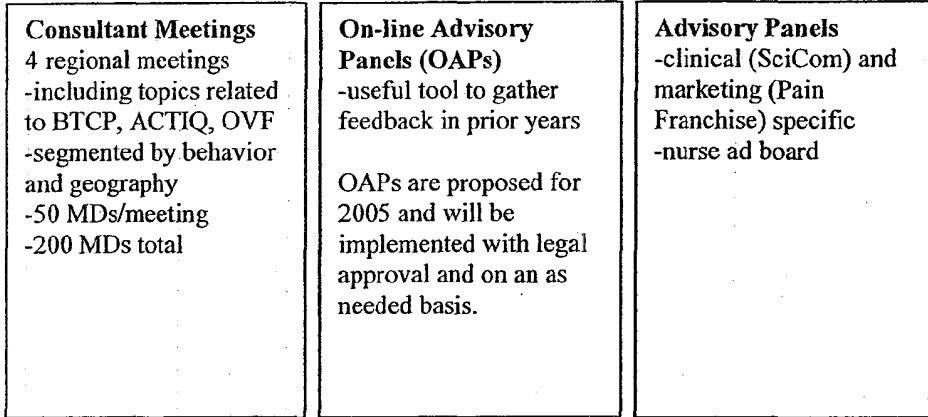
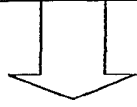
- Promotional Tactics
- Medical Education Initiatives
- Advisory Tactics
- *Emerging Solutions in Pain* – A fourth category for the *Emerging Solutions in Pain* initiative has been added for 2005. This initiative will be run like a “brand within a brand” since it has its own set of tactics.

The following is a brief overview and description of the 2005 ACTIQ tactical plan. The 2005 Tactical Budget is attached as appendix 6.

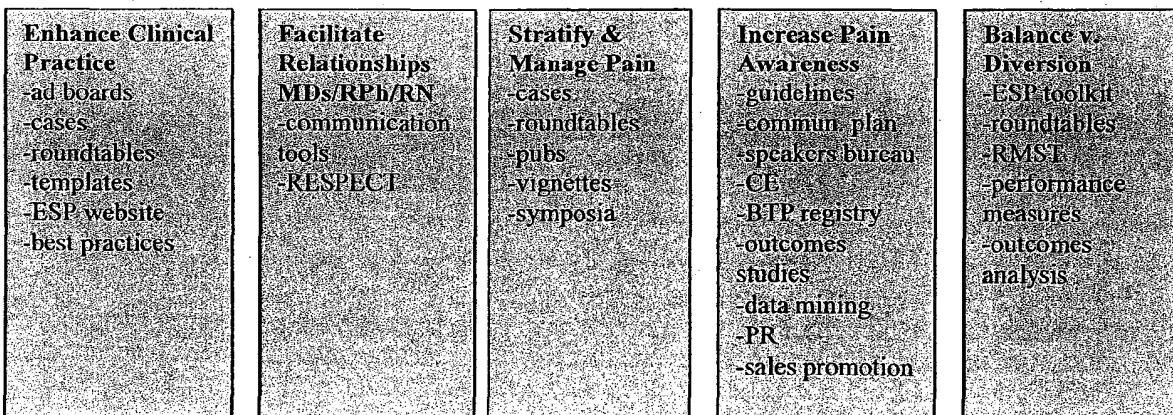
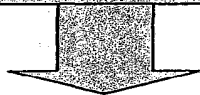
Also, the 2005 media plan and convention plan are attached as appendices 7 and 8.



**Advisory Tactics**



**Emerging Solutions in Pain Tactics**



Please refer to the CSF Table in appendix 9 that links the 2005 tactical plan to the 2005 critical success factors.

#### D. SUGAR FREE LAUNCH PLAN

##### *Objective*

Ensure a smooth transition to new sugar free formulation by minimizing disruption of sales and maximizing opportunity of sugar free ACTIQ (anticipated July 1, 2005).

##### *Issue*

Possible negative reaction from patients and prescribers and possible manufacturing issues with changeover to Sugar Free ACTIQ that could disrupt sales.

##### *Strategy*

Utilize all learnings from the negative reaction to the compressed powder formulation and better prepare the market for the sugar free reformulation.

More extensive pre-launch market research has been conducted in order to assess reaction to the new taste, texture and dissolvability of the sugar free formulation. This will help us prepare our messages and our launch materials to respond to or possibly avoid negative reaction. Marketing must also be conscious that there may be lingering negativity from the previous formulation change resulting in resistance to another change, therefore some market conditioning with positive messages must get out prior to launch. In order to minimize any interruption to ACTIQ sales, marketing will create and execute a thorough launch plan and will involve all relevant internal departments to ensure open communication to react quickly, should timelines change, or inventory and manufacturing issues arise. The launch plan will also map out how we plan to communicate the change to sugar free to all of our audiences, both internal and external.

##### *Vision*

Sugar free ACTIQ is the ideal first-line option to treat BTCP in opioid tolerant patients. (unchanged from ACTIQ vision)

##### *Positioning*

Sugar free ACTIQ's positioning will continue to focus on its key differentiating feature and benefit, with the additional benefit of sugar free.

- Key Feature: ACTIQ utilizes a unique oral transmucosal delivery system (OTS™) for rapid absorption of fentanyl
- Primary Patient Benefit: ACTIQ's oral transmucosal delivery system provides the most rapid onset of action among all non-invasive, shorter acting opioids.
- Secondary Patient Benefit: ACTIQ is sugar free and will not promote tooth decay (exact claims are still TBD)

### ***Launch Tactics***

Communications plan completed by Q4 2004 to deliver a consistent message to all audiences at launch (July 1, 2005):

- TSS
  - 3 months pre-launch - three wave direct mail campaign to educate the sales force about the benefits of the new sugar free formulation
    - W1 teaser
    - W2 product benefits & selling points
    - W3 preview of the new sales aids
  - 3 months pre-launch all sugar free training materials complete and TSS trained
  - 3 months pre-launch – sales force starts to disseminate sugar free placebos to prepare the market
  - At launch, all TSS will have sugar free versions of coupon books, dosing guides, core sales aids, along with a non-branded isomalt detail aid
- Journal Subscribers
  - 1-2 months pre-launch - announce the new formulation in all applicable professional journals
  - At launch update the brief summary with sugar free copy
- Physicians
  - At 2 months pre-launch, all ACTIQ prescribers contacted via fax and/or direct mail with sugar free information
  - 1 month pre-launch generate awareness and trial of new ACTIQ among current writers with a multiwave direct mail with sugar free teaser followed by a launch announcement offering a giveaway or coupons
  - At launch broadcast fax with sugar free announcement
  - At launch, new slim jim with sugar free ACTIQ FAQs provided to physicians by TSS
- Pharmacists
  - At 2 months pre-launch - all stocking pharmacies contacted via fax and/or direct mail with new NDC numbers and other sugar free information to
    - generate awareness of new ACTIQ among pharmacies that carry ACTIQ
  - At 2 months pre-launch - pharmlert insert to announce launch and new NDC codes (market research under way to determine the best way to get this type of information to pharmacists and their preferred method of communication)
  - At launch - broadcast fax with sugar free information and NDC codes
  - At 2 months pre-launch - screen saver and other materials – coordinated with commercial operations initiatives – distributed through wholesalers

- Patients
  - At launch - all ACTIQ patients to receive communication along with their ACTIQ prescription (for 3-5 months post launch) regarding change to sugar free to generate awareness of new ACTIQ
  - At launch – patient FAQ slim jim with information on change to ACTIQ to be distributed to patients by physicians and pharmacists
  - At launch - packaging stickers placed on all ACTIQ prescriptions
- Internal Cephalon
  - At 3 months post launch - sugar free information added to all sales aids
  - At launch - non-branded flashcard on Isomalt ready for TSS dissemination
  - At launch - PI/PL ready with new information
- Investors
  - At launch - PR to help communicate to investors via press releases
- Speakers Bureau
  - At launch - Professional Services to send letter to speakers bureau regarding change to sugar free ACTIQ
  - At launch - new slides added to promotional slide kit and/or slide kit developed on isomalt and posted to speaker extranet
  - New slides covered at 2005 speaker training meetings

Following launch all promotional materials will be updated and reprinted with the sugar free information.

***Sugar Free ACTIQ forecast***

No change in target sales or TRx goals since the sugar free launch is simply a replacement product for ACTIQ.

**E. ACTIQ 2005 MARKET RESEARCH PLAN**

***Yearly Projects***

- **Market Dynamics Study**
  - Understand how the current drivers and perceptions of ACTIQ and competitors have changed over the past year
  - Understand how customers are utilizing ACTIQ
  - Awareness and usage measures
- **Patient Chart Study**
  - Understand ACTIQ use by strength, disease state, and therapy strategy
- **ACNielsenHCI**
  - Measurement of ACTIQ journal concepts
- **Patient Flow Analysis**

- Capture patient utilization of ACTIQ compared to competitors
- **Speaker Content Study**
  - Study to evaluate / improve speaker materials
- **Opioid abuser study**
  - Understand physician tools for safeguarding against abuse and Abuse methods for circumventing these preventive measures
- ***Strategic Market Research Projects***
- **New User Analysis**
  - Understand how new users and targets perceive the message and the experience of using ACTIQ
- **Patient Research**
  - Understand patients' experiences with BTCP and beliefs and experiences using ACTIQ
- **Patient Segmentation**
  - Understand the mix of ACTIQ prescribers and potential patients
- **Customer Gap Analysis**
  - Understand differences in ACTIQ experience and BTCP that exist between physicians and patients
- **Reimbursement assessment**
  - Identify techniques that have been successful in gaining ACTIQ reimbursement
- ***Lifecycle Management***
- **Life-cycle Strategy Assessment**
  - Model impact of generic competitors and new branded competitors in order to quantify decision making process

## F. PUBLIC RELATIONS PLAN UNDER CONSIDERATION

In 2004, public relations activities continued to turn relationships with key stakeholders into tangible outcomes. Cephalon's visibility in the pain and oncology community is growing, and third-party patient and professional groups are increasing their own focus on BTCP.

The 2005 plan builds on these successes, looking strategically at opportunities to enhance Cephalon's image as a partner in pain management; increase BTCP and ACTIQ awareness in the pain and oncology communities; spotlight BTCP as a distinct pain syndrome; highlight ACTIQ as the only approved treatment for BTCP; and maintain an environment that is receptive for BTCP treatment with ACTIQ.



The core tactical initiatives for the 2005 ACTIQ PR plan are designed to:

- Strengthen ACTIQ-specific issues management initiatives
- Extend patient and professional awareness of BTCP
- Continue to build professional consensus about the need to assess and manage BTCP
- Maintain relationships with third-party organizations and key opinion leaders

#### *Issues Management Initiatives*

In Q3 and Q4 2004, several tactics will be implemented to improve Cephalon's ability to respond to media interest in ACTIQ. Designated spokespersons will be trained and media messages will continue to be refined. Meetings will be held with key reporters to improve the media's understanding of ACTIQ's safety and role in treating BTCP. Video footage will be created to provide a means of responding to broadcast media. The ACTIQ press kit will be reviewed and enhanced. In 2005, we will continue with activities such as:

- Proactive Preparation for Media Interaction:

Continue and expand activities initiated in 2004. Identify opportunities to communicate about risk minimization strategies implemented by the company.

- Third-Party Dialogue – “Common Ground Conference”:

Support convening of an independent group representing interested professional societies (pain, addictionology), advocacy groups (pain patients, drug prevention), industry, law enforcement, and regulators to discuss issues related to diversion, abuse, and misuse.

- ACTIQ Sugar-Free Formulation:

Facilitate a smooth introduction and acceptance of the new ACTIQ formulation by proactively informing key opinion leaders, professional and patients groups, and the trade media.

#### *Patient and Professional Awareness of BTCP*

The PR plan incorporates specific ideas to extend BTCP awareness among patients and clinicians. The majority of these programs will be implemented through unrestricted educational grants or contributions to third-party organizations.

The thematic concept that encircles most of the 2005 activities – “The Plain Talk about Pain Talk” – emphasizes: (1) patient/clinician communication about components of chronic pain; (2) real patient stories to illustrate the impact of BTCP and appropriate BTCP management on patient outcomes; and (3) opportunities to selectively engage the consumer media to drive positive stories about chronic pain management.

- Local Consumer Media Campaign Linked to “Community Service” Events:

Generate local, positive media attention in 2 medium-sized markets through a local celebrity spokesperson with a chronic pain experience, who will participate in local educational/support activities directed toward cancer patients with pain and their caregivers.

- Controlled Media Activities:

Deliver key messages to consumers via discrete media mechanisms such as radio media tours, audio news releases, matre features, and a web chat on a major health site.

- American Pain Foundation TARGET Chronic Pain Tools:

Support increased visibility and use of APF-developed educational tools – the Clinician Card and the Patient Pain Tracker – to enhance awareness of BTCP.

- Identify mechanisms to expand distribution of the Patient Pain Tracker (diary) either directly to consumers or through health care providers, including support for APF web-based programs and increased attendance by the Foundation at consumer and medical meetings.
- Convert Clinician Card into PDA software that can be downloaded from the website of a professional society.
- Provide an unrestricted educational grant for APF to conduct a session as part of the agenda of the 2005 meeting of the American Society for Pain Management Nursing. Highlight value of tools in management of persistent and Breakthrough Cancer Pain.

- Speaker Slide Kit “Put the Brakes on BTCP”

Roll-out production and distribution of speaker kit/video developed in Q3-Q4 2004 and tailored to presentations to patients/caregivers. Distribute to active community speakers to enhance their discussion of BTCP and treatment options.

- Skill-Building Teleconference on Patient/Clinician Communication

Enhance oncologists’ recognition of tools available to improve patient/clinician communication related to pain management through support of a *CancerCare* teleconference.

- Journal Articles

Encourage thought leaders from the Nurses Advisory Board to write articles related to resources available to facilitate patient/clinician communication about chronic pain. Direct messages to advance practice nurses, palliative care, hospice, and clergy.

***Professional Consensus***

In Q3-Q4 2004, a roundtable will be convened under the auspices of a professional society to bring together leaders from organizations representing pain management experts, oncologists, and patient advocacy groups to develop a consensus statement

regarding the definition of BTCP and what is required to improve assessment and management of this condition.

- BTCP Roundtable

Disseminate call to action to participating groups' membership and promote messages to media.

*Third-Party Organizations and Key Opinion Leaders*

- Constituency Group Support – Opportunistic Initiatives

Provide corporate contributions and unrestricted educational grants to advocacy/professional societies to promote interest and education related to awareness and management of components of chronic pain and patient/clinician communication.

- Nurses Advisory Board

Seek counsel for and participation in selected activities supported under the PR plan. Coordinate meeting to identify continuing needs of the professional and consumer communities and set program directions for future activities.

- Professional Meetings

Interact with thought leaders at key professional society meetings to maintain Cephalon's position as a player and partner, and increase attention on BTCP and ACTIQ.

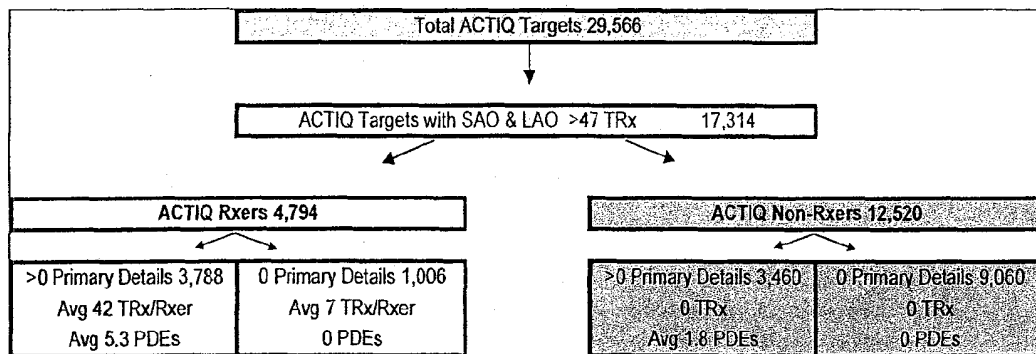
## **VII. Appendix**

- 1. Target analysis**
- 2. Table of Long-Acting Opioids and Short-Acting Pure Opioids**
- 3. Potential Competitors**
- 4. Proposed Concept Journal Ad**
- 5. Current Concept Journal Ad**
- 6. 2005 Tactical Budget**
- 7. 2005 Media Plan**
- 8. 2005 Medical Meeting Plan**
- 9. Table of CSF Linked to Tactics**

## APPENDIX 1 Highest Potential AB Targets

### LAO and SAO Analysis

The following illustration divides ACTIQ targets into users and non-users by applying a stringent criteria of minimal prescribing levels of both long acting opioids - LAOs (>47 TRx in the last six months) and short-acting opioids - SAOs (>47 TRx in the last six months). The users and non-user groups are further divided into sub-groups based on call activity during this same time period. This top-line look at users and non-users classified based on high prescribing levels of both LAOs and SAOs and call activity shows that those physicians meeting these high prescribing standards who receive calls are far more productive ACTIQ prescribers than those who receive few or zero calls.



This top-line illustration begs an additional question: do the users and non-users truly look the same (exhibit the same prescribing behavior)?

Below are two tables showing the 4,794 ACTIQ users and 12,520 non-users based on SAO and LAO prescribing deciles. The highlighted areas on both tables compare the ACTIQ users to the non-users. Looking at the two groups, the ACTIQ prescribers write at high levels of LAOs, or if their LAO writing is less than a decile 10 they also write at high levels of SAOs. The non ACTIQ prescribers (highlighted on the second table) are concentrated at the lower deciles of LAOs.

The area on the second table with bold red numbers shows that there are still 3,725 non-users that look like the 2,699 high prescribing users and may have the potential to become ACTIQ users. This is only one analysis using LAOs and SAOs as markers and more information about the 3,725 is necessary. Perhaps they differ attitudinally and have different needs in order to become ACTIQ prescribers. They may be more influenced by the external factors mentioned previously. Perhaps they need more sales force time and effort or require different messaging. In order to determine why this is, two primary market research projects are currently underway. The first is to understand the drivers and barriers to physician usage of ACTIQ based on an in-depth understanding of what motivates physician usage patterns. Specific questions such as "why have you increased / decreased your ACTIQ writing?" will be addressed, as well as determining exactly what key messages led to an increase in ACTIQ writing. A second research project was conducted in order to segment physicians according to treatment behaviors, attitudes

toward pain, product attribute preferences, demographic information, geographic and other distinguishing characteristics. Results of both of these projects are expected in Q4 2004, and will help marketing plan promotional efforts and messages specific to this segment.

**ACTIQ Targets - Writers**  
**Long Acting Opioid Decile TRx Count Feb - Jul 2004**

	10	9	8	7	6
<b>10</b>	301	306	160	53	26
<b>9</b>	38	242	288	159	72
<b>8</b>	1	75	201	161	113
<b>7</b>	0	21	100	174	120
<b>6</b>	0	15	63	123	136
<b>5</b>	1	1	21	80	115
<b>4</b>	0	3	10	51	95
<b>3</b>	0	0	4	16	79
<b>2</b>	0	0	3	6	30
<b>1</b>	0	0	0	0	0

Short Acting Opioid\*  
 Decile TRx  
 Count Feb - Jul 2004

**ACTIQ Targets - Non-Writers**  
**Long Acting Opioid Decile TRx Count Feb - Jul 2004**

	10	9	8	7	6
<b>10</b>	40	94	156	210	135
<b>9</b>	8	50	189	344	333
<b>8</b>	7	21	156	336	440
<b>7</b>	1	10	75	286	476
<b>6</b>	1	4	43	200	474
<b>5</b>	0	2	25	128	409
<b>4</b>	0	1	7	79	280
<b>3</b>	0	1	9	48	220
<b>2</b>	0	1	1	22	75
<b>1</b>	0	0	0	0	2

Short Acting Opioid\*  
 Decile TRx  
 Count Feb - Jul 2004

Highlighted non-ACTIQ Rxing targets do not exhibit similar Rxing behavior to high ACTIQ Rxing targets

**Bolded red non-ACTIQ Rxing targets exhibit similar Rxing behavior to high ACTIQ Rxing targets, representing opportunity**

\*\*Short Acting Opioid Market includes Hydrocodone, Hydromorphone, Oxycodone and Morphine Sulfate

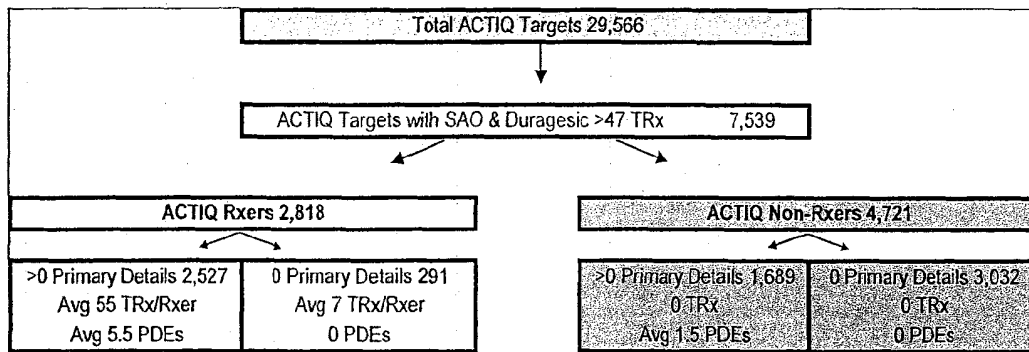
The 3,75 targets who are non-writers who exhibit similar prescribing behavior to the high prescribing users will be identified and provided to the sales force, along with the appropriate message.

***Duragesic and SAO Analysis***

The following information replicates the previous analysis on LAOs and SAOs as indicators of areas for growth opportunity. This analysis uses a specific LAO – Duragesic and SAOs. As with the previous analysis, this top-line look at users and non-users and call activity shows that those physicians who receive calls are far more productive ACTIQ prescribers than those who receive few or no calls.

Again, the ACTIQ targets are divided into users and non-users by applying the same criteria of Duragesic (>47 TRx in the last six months) and short-acting opioids (>47 TRx in the last six months). The users and non-user groups are further divided into sub-groups based on call activity during this same time period, and also shows that those physicians who receive calls are far more productive ACTIQ prescribers than those who receive few or zero calls.

**User versus Non-user – Duragesic and SAO Analysis  
(Feb-Jul 2004)**



Below are two tables showing the 2,818 ACTIQ users and 4,721 non-users based on SAO and Duragesic prescribing deciles (2 markers used to determine ACTIQ targets). The highlighted areas on both tables compare the ACTIQ users to the non-users. Looking at the two groups, the ACTIQ prescribers write at high levels of Duragesic, or if their Duragesic writing is less than a decile 10 they also write at high levels of SAOs. The non ACTIQ prescribers (highlighted on the second table) are concentrated at the lower deciles of Duragesic and SAOs.

The area on the second table with bold red numbers shows that there are still 2,213 non-users that look like the 2,086 high prescribing users and may have the potential to become ACTIQ users. Again, this is only one analysis using certain markers and more information about the 2,213 is necessary which will be discovered during market research. Once the appropriate message for this segment is identified, they will be provided to the sales force.

**ACTIQ Targets - Writers**

**Duragesic Decile TRx Count Feb - Jul 2004**

Short Acting  
Opioid\*  
Decile TRx  
Count Feb -  
Jul 2004

	10	9	8	7	6
10	270	268	145	85	23
9	60	216	220	139	57
8	16	90	142	118	56
7	4	33	98	124	43
6	3	20	56	111	42
5	0	8	36	74	38
4	1	3	14	51	45
3	0	1	11	37	31
2	0	1	2	18	15
1	0	0	0	1	3

**ACTIQ Targets - Non-Writers (4,763 Prescribers)**

**Duragesic Decile TRx Count Feb - Jul 2004**

Short Acting  
Opioid\*  
Decile TRx  
Count Feb -  
Jul 2004

	10	9	8	7	6
10	35	75	158	168	81
9	16	79	192	262	158
8	7	57	180	304	185
7	4	22	143	300	227
6	0	17	96	244	230
5	0	8	97	224	202
4	0	4	38	189	184
3	0	10	35	153	145
2	0	2	16	84	119
1	0	0	1	8	4

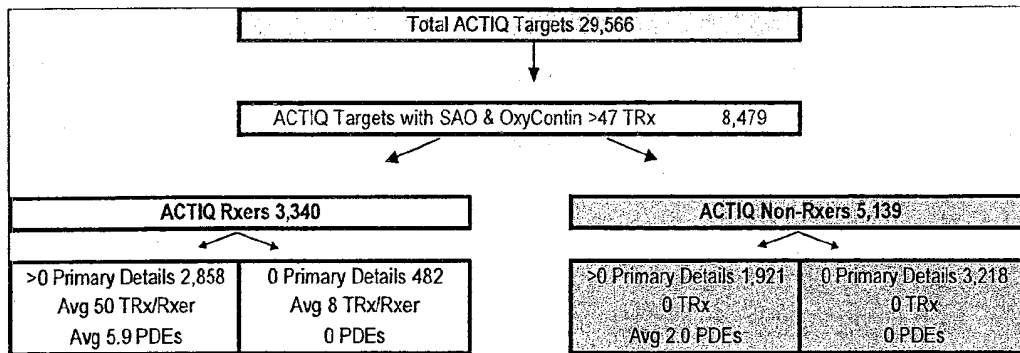
Highlighted non-ACTIQ Rxing targets do not exhibit similar Rxing behavior to high ACTIQ Rxing targets

Bolded red non-ACTIQ Rxing targets exhibit similar Rxing behavior to high ACTIQ Rxing targets, representing opportunity

***OxyContin and SAO Analysis***

The following information replicates the two previous analyses evaluating areas for growth opportunity. This analysis uses OxyContin and SAOs. As with the previous analyses, those physicians who receive calls are far more productive ACTIQ prescribers than those who receive few or no calls.





Below are two tables showing the 3,340 ACTIQ users and 5,139 non-users based on SAO and OxyContin prescribing deciles. The highlighted areas on both tables compare the ACTIQ users to the non-users. Looking at the two groups, the ACTIQ prescribers write at high levels of OxyContin, or if their OxyContin writing is less than a decile 10 they also write at high levels of SAOs. The non ACTIQ prescribers (highlighted on the second table) are concentrated at the lower deciles of OxyContin and SAOs. This is similar to the previous 2 analyses.

The area on the second table with bold red numbers shows that there are still 1,850 non-users that look like the 1,940 high prescribing users and may have the potential to become ACTIQ users. More information is needed about the 1,850 which will be found in market research. Once the appropriate message for this segment is identified, they will be provided to the sales force.

**ACTIQ Targets - Writers**  
**OxyContin Decile TRx Count Feb - Jul 2004**

	<b>10</b>	<b>9</b>	<b>8</b>	<b>7</b>	<b>6</b>
<b>10</b>	245	284	162	66	33
<b>9</b>	30	199	249	154	82
<b>8</b>	3	66	148	138	116
<b>7</b>	2	11	84	115	130
<b>6</b>	1	5	62	80	92
<b>5</b>	1	4	20	41	78
<b>4</b>	0	3	5	41	70
<b>3</b>	0	1	2	15	46
<b>2</b>	0	0	0	9	11
<b>1</b>	0	0	0	0	1

Short Acting Opioid\*  
 Decile TRx  
 Count Feb - Jul 2004

ACTIQ Targets - Non-Writers  
 OxyContin Decile TRx Count Feb - Jul  
 2004

	10	9	8	7	6
10	48	92	132	142	98
9	11	66	161	241	205
8	6	31	136	212	284
7	0	14	89	188	290
6	1	7	51	162	268
5	0	7	23	99	196
4	0	1	12	63	162
3	0	1	8	34	113
2	0	1	3	14	44
1	0	0	0	0	2

Short Acting  
 Opioid\*  
 Decile TRx  
 Count Feb -  
 Jul 2004

Highlighted non-ACTIQ Rxing targets do not exhibit similar Rxing behavior to high ACTIQ Rxing targets

Bolded red non-ACTIQ Rxing targets exhibit similar Rxing behavior to high ACTIQ Rxing targets, representing opportunity

\*\*Short Acting Opioid Market includes Hydrocodone, Hydromorphone, Oxycodone and Morphine Sulfate

**APPENDIX 2 Long-Acting Opioids and Short-Acting Pure Opioids**

<b>Long Acting Opioids</b>			
<b>Opiumid</b>	<b>Trade Name</b>	<b>Generic Name</b>	<b>Manufacturer</b>
Fentanyl	Duragesic	Fentanyl Transdermal System	Janssen
Oxycodone	OxyContin	Oxycodone HCL CR	Purdue Pharma
Morphine	Oxycodone ER (Gen.)		Teva
	MSContin	Morphine Sulfate	Purdue Pharma
	Oramorph	Morphine Sulfate	Roxane
	Kadian	Morphine Sulfate	Faulding
	Avinza	Morphine Sulfate	Ligand
	Generics (3)	Morphine Sulfate	3 companies
<b>Short Acting Pure Opioids</b>			
<b>Opiumid</b>	<b>Trade Name</b>	<b>Generic Name</b>	<b>Manufacturer</b>
Fentanyl	ACTIQ	Oral Transmucosal Fentanyl Citrate	Cephalon
Oxycodone*	OxyIR	Oxycodone HCl Immediate-Release	Purdue Pharma
	OxyFast	Oxycodone HCl Immediate-Release	Purdue Pharma
	Roxicodone	Oxycodone HCl	Roxane
Morphine*	Oxydose	Oxycodone HCl	Ethex Corp.
	MSIR	Morphine Sulfate	Purdue Pharma
Hydromorphone*	Roxanol	Morphine Sulfate	Roxane
	Dilaudid	Hydromorphone HCl	Knoll/Abbott Labs
	Palladone	Hydromorphone HCl	Purdue Pharma

\*Generic forms of short acting morphine, oxycodone and hydromorphone also exist.

APPENDIX 3 Potential Competitors

Company	Product	Phase	Comments
Endo/Penwest	Oxymorphone Immediate Release	Received approvable letter in Oct. 03. Estimated launch 1Q 2006	Still negotiating with FDA on design of second trial
ALZA (JNJ)	Ionsys (E-trans)	Estimated launch 4Q 2005	Company has stated that the product targets the market currently served by IV patient controlled morphine delivery systems. The indication is for in-hospital postoperative pain.
Biovail	Ralivia Flash dose (tramadol orally-disintegrating tablet)	Indication for moderate to severe pain filed on 3/24/04	Reported that need for slow titration in dosage when initiating tramadol limits its use for the treatment of acute pain. Tramadol's brand name is Ultram
Endo	Rapinyl	Indicated for the treatment of breakthrough cancer pain.	As of August 2004, Rapinyl was in Phase II clinical trials. Phase III are schedule to begin in 2005
Aradigm/GSK	AERx (inhaled morphine) for acute pain and BTP	Two Phase IIb completed which demonstrated safety, efficacy and dose reproducibility comparable to IV morphine	PIII studies were contingent on GSK recommitting to the program or a new partner entering the agreement. GSK has not recommitted so <u>development is currently on hold.</u>
Delex	AeroLEF (pulmonary inhalation fentanyl)	Phase IIa completed 6/9/04 in post-surgical athletes (CAN)	Sustained therapeutic plasma concentrations that mimic the longer duration of action normally associated with slow onset products
QRxPharma	Immediate release "novel opioid + opioid sparing"	Currently in Phase II but company has plans for starting Phase III study by end of 2004	Patent information indicates that this is a oxycodone and morphine combination
Nastech / Pfizer	Nasal systemic formulation of morphine gluconate	Phase II Break-through Pain completed looking for partner to complete development	Phase II study showed that intranasal morphine gluconate was rapidly absorbed, with onset of pain relief at an average of 2.2 min post dosing and meaningful pain relief of 9.1 min
Orexo / Diabact fka	Rapinyl (KW-2246) / Sublingual tablet	Phase II in Sweden	Patented drug delivery platform for sublingual administration resulting in rapid absorption and onset of action. The drug is also in development in Japan

APPENDIX 4 Proposed Concept Journal Ad



**ACTIQ AND OTHER HERIATINE PRODUCTS MUST BE USED EXACTLY WITH THE DIRECTIONS INDICATED IN THIS LABEL.**

As this medication is used for the management of breakthrough cancer pain in patients with end-stage cancer, it is not intended for use in patients who are not taking opioid analgesics for their underlying, persistent cancer pain. Patients receiving oral opioid analgesics are at risk for respiratory depression, hypotension, loss of consciousness, or coma if they take too much of this medication. Because the respiratory depression could occur at any dose in patients not taking chronic opioids, Actiq is contraindicated in the management of a state of respiratory depression. This product must not be used in patients with acute pain.

Actiq is indicated to be used only in the case of cancer patients and only by oncologists and pain specialists who are knowledgeable of and familiar with the use of Schedule II opioid medications.

Patients and their caregivers must be instructed that Actiq contains a medicine in an amount which can be fatal to a child. Patients and their caregivers must be instructed to keep all units out of the reach of children and to discard open units properly. (See Information for Patients and Their Caregivers for disposal instructions.)

Please see boxed warning and full summary of prescribing information on adjacent pages. For more information, please call Cephalon Professional Services at 1-800-876-1825.

**When onset matters... ACTIQ responds.**

The main benefit of ACTIQ is its time to onset of analgesia.

- Without a wait time, ACTIQ provides relief of cancer pain in minutes, not hours.
- ACTIQ is a fast-acting, non-opioid analgesic that can be used in patients who are already taking opioids for their cancer pain.
- High bioavailability and immediate onset of action allow for rapid relief of breakthrough cancer pain.
- The unique oral transmucosal delivery system (OS) allows for easy administration, is highly palatable and easy to swallow, and is safe.
- Long-acting oral opioids are used for baseline cancer pain, while ACTIQ provides fast relief of breakthrough cancer pain.

**Safety**

- Not intended for use in patients with acute pain or non-cancer pain.
- Be aware of other drugs that may interact with ACTIQ. Avoid alcohol, sedatives, and other CNS depressants.
- Use of ACTIQ units has been reported to cause respiratory depression.

**Portability and convenience**

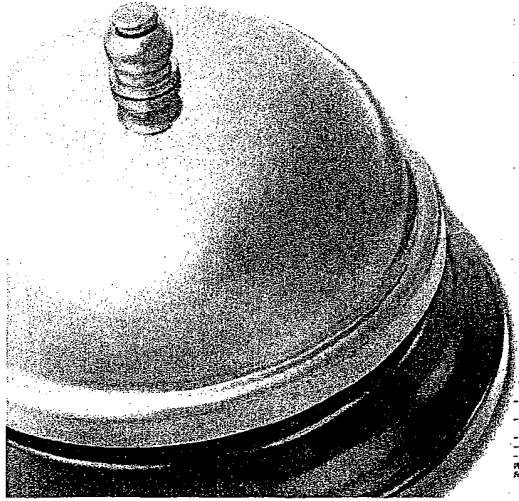
- Patients can use ACTIQ anywhere, anytime, even when they begin to feel breakthrough cancer pain.



Relief at hand

When onset matters...

Actiq on call.



With ACTIQ, pain relief may be observed in 15 minutes.<sup>1</sup>

**Rapid transmucosal absorption**

- The unique oral transmucosal system (OTS™) of ACTIQ allows for rapid oral transmucosal absorption and allows for absorption of fentanyl.
- Patients may begin experiencing pain relief while using ACTIQ, but may not experience full relief for up to 45 minutes after loading an ACTIQ unit.
- Analgesic effects of fentanyl are related to blood level, with delay into onset of the CNS in process with a 3- to 5-minute half life.<sup>1</sup>
- Longer or shorter onset times may occur than the recommended 15 minutes may predict. Use always as reported in clinical trials.

**No pharmacologically active metabolites**

- Safety and efficacy have been established in opioid tolerant patients receiving both long-acting oral and transmucosal opioids.<sup>2</sup>

**Typical opioid side effects**

- The most common side effects observed were somnolence, nausea, vomiting, and dizziness.

**Portability, convenience, control**

- The oral transmucosal delivery system and onset of action of ACTIQ provide patients with portability, convenience, and control.



**Important Warnings**

- Indicated only for the management of breakthrough cancer pain in patients with malignancies who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain.
  - Because the therapeutic effectiveness could occur at any time in patients not taking chronic opioids, ACTIQ is contraindicated in the management of acute or postoperative pain.
  - This product must not be used in opioid-naïve patients.
  - Inherent patient/caregiver risk: ACTIQ can be used in a child. Keep all units from children and use properly.
  - The most common side effects observed in ACTIQ clinical trials were somnolence, nausea, vomiting, and dizziness. Please see local labeling and local regulatory procedures for complete on-adult patient.
- For more information, please call Cephalon Professional Services at 1-800-856-5855.

APPENDIX 6 2005 ACTIQ Tactical Budget

2005 Budget Categories	Amount	Rationale
Market Research	\$ 1,000,000	Per Market Research requirements
Consultants	\$ 100,000	Much needed medical-strategic support
Journal Reprints	\$ 525,000	
Convention	\$ 948,383	Increased presence at pain congresses
Advertising/Promotional Materials	\$ 5,602,300	New concept launch and sugar free launch
Integrated Communication Plan	\$ 100,000	Support field based promotion
Sample Coupons	\$ 1,932,500	Support of current sales force size
Public Relations	\$ 500,000	Increased media attention/new data
Field Driven MEPS	\$ 5,000,000	Support of current sales force size
Medical Education	\$ 9,070,000	Support CME, consultant meetings, spkr training
Corporate Contributions	\$ 200,000	Increased support to pain community
RMP Requirements	\$ 282,000	Modernization, increased welcome kit activity
ESP	\$ 2,000,000	
<b>Total</b>	<b>\$ 27,300,000</b>	

**APPENDIX 7 2005 Media Plan**

	Totals	Q1 2004	Q2 2004	Q3 2004	Q4 2004
Number of Insertions	143	36	34	39	34
Avg. Exposures per MD	165.7	41.4	41.4	41.5	41.4
Total Journal Investment	\$980,831	\$265,090	\$216,681	\$275,341	\$223,719
Estimated CMI Fee	\$72,250				
Total Investment	\$1,053,331				

	Spend	# Insertions Q1	# Insertions Q2	# Insertions Q3	# Insertions Q4	Total Insertions
<b>ANESTHESIOLOGY</b>						
Anesthesia & Analgesia	\$62,814	6	6	6	6	24
Anesthesiology	\$114,651	6	6	6	6	24
Anesthesiology News	\$154,224	3	3	4	3	16
<b>ONCOLOGY</b>						
Am Jrl of Oncology Review	\$155,670	2	1	2	1	6
Oncology Net Guide	\$82,010	1	2	2	3	8
Jrl of Am Med Assn-Cancer Demo	\$68,972	3	3	3	3	12
Jrl of Supportive Oncology	\$75,238	2	1	2	1	6
<b>PAIN SPECIALIST</b>						
Jrl of Pain	\$28,917	2	3	2	2	9
Jrl of Pain Symptom Mgmt	\$85,064	3	3	3	3	12
Pain Medicine	\$12,943	1	1	1	1	4
Pain Medicine News	\$97,059	3	1	3	1	8
Practical Pain Mgmt	\$43,268	2	1	2	1	6



**APPENDIX 8 2005 Medical Meeting Plan**

NAME & DATE	PRODUCT	WEBSITE	SPECIALTY/ ATTENDEE #
<b>AAHPM</b> Amer. Academy of Hospice & Palliative Med January 19-23 New Orleans, LA	ACTIQ	<a href="http://www.aahpm.org">http://www.aahpm.org</a>	<b>Palliative Care</b> <b>500</b>
<b>AAPM</b> American Academy of Pain Medicine February 23-27 Palm Springs, CA	GAB/ ACTIQ	<a href="http://www.painmed.org">http://www.painmed.org</a>	<b>Pain</b> <b>600</b>
<b>APS</b> Amer. Pain Society March 30-April 2 Boston, MA	GAB/ ACTIQ	<a href="http://www.ampainsoc.org">http://www.ampainsoc.org</a>	<b>Pain</b> <b>2,000</b>
<b>ASPMN</b> American Society for Pain Mgmt Nurses March 31-April 3 Albuquerque, NM	ACTIQ	<a href="http://www.aspmn.org">www.aspmn.org</a>	<b>Pain</b> <b>600</b>
<b>AAN</b> American Academy of Neurology April 9-16 Miami Beach, FL	PROV/ GAB/ ACTIQ	<a href="http://www.aan.com/">http://www.aan.com/</a>	<b>Neuro</b> <b>10,000</b>
<b>AMCP</b> Academy of Managed Care Pharmacy April 20-23 Denver, CO	ACTIQ	<a href="http://www.amcp.org">www.amcp.org</a>	<b>Pharmacists</b> <b>3000</b>
<b>ONS</b> Oncology Nursing Society April 28-May 1 Orlando, FL	ACTIQ	<a href="http://www.ons.org">www.ons.org</a>	<b>Oncology</b> <b>8,500</b>
<b>ASCO</b> American Society of Clinical Oncology May 14-17 Orlando, FL	ACTIQ/ PROV	<a href="http://www.asco.org">www.asco.org</a>	<b>Oncology</b> <b>22,000</b>

**APPENDIX 8 2005 Medical Meeting Plan (cont'd)**

NAME & DATE	PRODUCT	WEBSITE	SPECIALTY/ ATTENDEE #
<b>ASHP</b> American Society of Health-System Pharmacists June 11-15 Boston, MA	ACTIQ	<a href="http://www.ashp.org">www.ashp.org</a>	Pharmacists
<b>AAPM</b> Amer. Academy of Pain Management	GAB/ ACTIQ	<a href="http://www.aapainmanage.org">www.aapainmanage.org</a>	Pain 800
<b>IASP</b> International Association for the Study of Pain August 21-26 Sydney, Australia	ACTIQ	<a href="http://www.iasp-pain.org">www.iasp-pain.org</a>	Pain
<b>AAFP</b> American Academy of Family Physicians September 28-October 2 San Francisco, CA	ACTIQ	<a href="http://www.aafp.org">www.aafp.org</a>	FP 20,000
<b>ASTRO</b> Amer. Society for Therapeutic Radiology & Oncology October 16-20 Denver, CO	ACTIQ	<a href="http://www.astro.org">www.astro.org</a>	Oncology 9,000
<b>AAPM&amp;R</b> Amer. Academy of Physical Medicine & Rehab October 27-30 Philadelphia, PA	ACTIQ	<a href="http://www.aapmr.org/">http://www.aapmr.org/</a>	2,000
<b>ONS</b> Oncology Nursing Society – Institutes of Learning	ACTIQ	<a href="http://www.ons.org">www.ons.org</a>	

APPENDIX 9 CSF Table

	CSF #1 Sales Force support & motivation	CSF #2 Smooth transition to ACTIQ SF formulation	CSF #3 BTCP & ACTIQ awareness	CSF #4 Reimbursement tools	CSF #5 Increased comfort Rxing opioids	CSF #6 KOL increase BTCP awareness
<b>PROMO TACTICS:</b>						
New concept detail aids	X					
coupons	X					
BTP assessment tool/poster	X		X			
RMP sales aid	X				X	
ESP sales aid toolkit, MEPs	X				X	
Promo/WEF reprints	X					
Giveaways	X					
Convention presence		X	X			
Revised booth animation video	X		X			
Fentanyl MOA video or pain pathophys video	X					
ACTIQ.com	X	X				
Journal ads			X			
Speaker training	X	X	X	X		X
All sugar free tactics	X	X				
<b>MEDED TACTICS:</b>						
MEPs	X		X		X	
CME programs			X		X	X
Publications	X		X	X	X	X
<b>ADVISORY TACTICS:</b>						
Consultant mtgs for advice on			X	X	X	X
OAPs for feedback on			X	X	X	X
Adv panels for advice on			X	X	X	X

	CSF #1 Sales Force support & motivation	CSF #2 Smooth transition to ACTIQ SF formulation	CSF #3 BTCP & ACTIQ awareness	CSF #4 Reimbursement tools	CSF #5 Increased comfort Rxing opioids	CSF #6 KOL increase BTCP awareness
ESP TACTICS:						
Advisory Panels					X	X
Roundtables					X	X
ESP.com	X				X	X
RESPECT mtgs					X	X
Publications	X			X	X	X
Symposia					X	X
BTP Guidelines				X	X	X
Speakers bureau					X	X
CE					X	X
BTP registry					X	X
PR Efforts					X	X
ESP toolkit	X				X	X
RMST					X	X