# Exhibit 1

JANE - FILE TAB FOR SUBJECT - QUARTERLY REPORT

# memo

EDWARD W. ALBRIGHT

APR 28 1994

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to: Distribution

from: Jonathan D. Sackler

dept:

subject:

date: April 26, 1994

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| | |
|---|---|
| To Ed Albright | From Jon Sackler |
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| Dept. | Phone # 4/26/94 |
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✓ [illegible] for meetings

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# Exhibit 2

# OxyContin™ 10 mg Tablets
# OxyContin™ 20 mg Tablets
# OxyContin™ 40 mg Tablets

(Oxycodone Hydrochloride Controlled-Release)

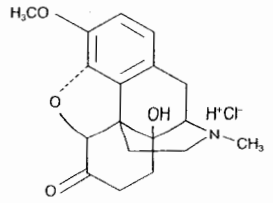
**C II**

## WARNING: May Be Habit Forming

A4909-811

### DESCRIPTION

OxyContin™ (oxycodone hydrochloride controlled-release) tablets are an opioid analgesic supplied in 10 mg, 20 mg, and 40 mg tablet strengths for oral administration. The tablet strengths describe the amount of oxycodone per tablet as the hydrochloride salt. The structural formula for oxycodone hydrochloride is as follows:




$C_{18}H_{21}NO_4 \cdot HCl$ MW 351.83

The chemical formula is 4, 5-epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride.

Oxycodone is a white, odorless crystalline powder derived from the opium alkaloid, thebaine. Oxycodone hydrochloride dissolves in water (1 g in 6 to 7 mL). It is slightly soluble in alcohol (octanol water partition coefficient 0.7). The tablets contain the following inactive ingredients: ammonio methacrylate copolymer, hydroxypropyl methylcellulose, lactose, magnesium stearate, povidone, red iron oxide (20 mg strength tablet only), stearyl alcohol, talc, titanium dioxide, triacetin, yellow iron oxide (40 mg strength tablet only), and other ingredients.

### CLINICAL PHARMACOLOGY

*Central Nervous System*

Oxycodone is a pure agonist opioid whose principal therapeutic action is analgesia. Other therapeutic effects of oxycodone include anxiolysis, euphoria and feelings of relaxation. Like all pure opioid agonists, there is no ceiling effect to analgesia, such as is seen with partial agonists or non-opioid analgesics.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and play a role in the analgesic effects of this drug.

Oxycodone produces respiratory depression by direct action on brain stem respiratory centers. The respiratory depression involves both a reduction in the responsiveness of the brain stem respiratory centers to increases in carbon dioxide tension and to electrical stimulation.

Oxycodone depresses the cough reflex by direct effect on the cough center in the medulla. Antitussive effects may occur with doses lower than those usually required for analgesia.

Oxycodone causes miosis, even in total darkness. Pinpoint pupils are a sign of opioid overdose but are not pathognomonic. Marked mydriasis rather than miosis may be seen due to hypoxia in overdose situations.

*Gastrointestinal Tract and Other Smooth Muscle*

Oxycodone causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone may be increased to the point of spasm resulting in constipation. Other opioid-induced effects may include a reduction in gastric, biliary and pancreatic secretions, spasm of sphincter of Oddi, and transient elevations in serum amylase.

*Cardiovascular System*

Oxycodone may produce release of histamine with or without associated peripheral vasodilation. Manifestations of histamine release and/or peripheral vasodilation may include pruritus, flushing, red eyes, sweating, and/or orthostatic hypotension.

*Concentration—Efficacy Relationships (Pharmacodynamics)*

Studies in normal volunteers and patients reveal predictable relationships between oxycodone dosage and plasma oxycodone concentrations, as well as between concentration and certain expected opioid effects. In normal volunteers these include pupillary constriction, sedation and overall "drug effect" and in patients, analgesia and feelings of "relaxation." In non-tolerant patients, analgesia is not usually seen at a plasma oxycodone concentration of less than 5–10 ng/mL.

As with all opioids, the minimum effective plasma concentration for analgesia will vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. As a result, patients need to be treated with individualized titration of dosage to the desired effect. The minimum effective analgesic concentration of oxycodone for any individual patient may increase with repeated dosing due to an increase in pain and/or the development of tolerance.

*Concentration—Adverse Experience Relationships*

OxyContin™ tablets are associated with typical opioid-related adverse experiences similar to those seen with immediate-release oxycodone and all opioids. There is a general relationship between increasing oxycodone plasma concentration and increasing frequency of dose-related opioid adverse experiences such as nausea, vomiting, CNS effects and respiratory depression. In opioid-tolerant patients, the situation is altered by the development of tolerance to opioid-related side effects, and the relationship is poorly understood.

As with all opioids, the dose must be individualized (see DOSAGE AND ADMINISTRATION), because the effective analgesic dose for some patients will be too high to be tolerated by other patients.

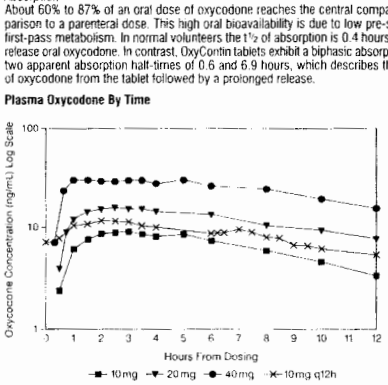
### PHARMACOKINETICS AND METABOLISM

The activity of OxyContin™ (oxycodone hydrochloride controlled-release) tablets is primarily due to the parent drug oxycodone. OxyContin tablets are designed to provide controlled delivery of oxycodone over 12 hours. Oxycodone is well absorbed from OxyContin tablets with an oral bioavailability of from 60% to 87%. The relative oral bioavailability of OxyContin to immediate-release oral dosage forms is 100%. Upon repeated dosing in normal volunteers, steady-state levels were achieved within 24-36 hours. Dose proportionality has been established for the 10 mg, 20 mg and 40 mg tablet strengths for both peak plasma levels ($C_{max}$) and extent of absorption (AUC). Oxycodone is extensively metabolized and eliminated primarily in the urine as both conjugated and unconjugated metabolites. The apparent elimination half-life of oxycodone following the administration of OxyContin was 4.5 hours compared to 3.2 hours for immediate-release oxycodone.

*Absorption*

About 60% to 87% of an oral dose of oxycodone reaches the central compartment in comparison to a parenteral dose. This high oral bioavailability is due to low pre-systemic and/or first-pass metabolism. In normal volunteers the $t_{1/2}$ of absorption is 0.4 hours for immediate-release oral oxycodone. In contrast, OxyContin tablets exhibit a biphasic absorption pattern with two apparent absorption half-times of 0.6 and 6.9 hours, which describes the initial release of oxycodone from the tablet followed by a prolonged release.

**Plasma Oxycodone By Time**




Dose proportionality has been established for the 10 mg, 20 mg and 40 mg tablet strengths for both peak plasma concentrations ($C_{max}$) and extent of absorption (AUC) (see Table 1 below). Given the short half-life of elimination of oxycodone from OxyContin, steady-state plasma concentrations of oxycodone are achieved within 24-36 hours of initiation of dosing with OxyContin tablets. In a study comparing 10 mg of OxyContin every 12 hours to 5 mg of immediate-release oxycodone every 6 hours the two treatments were found to be equivalent for AUC and $C_{max}$, and similar for $C_{min}$ (trough) concentrations. There was less fluctuation in plasma concentrations for the OxyContin tablets than for the immediate-release formulation.

**Table 1**

*Mean [% coefficient variation]*

| Regimen/ Dosage Form | AUC (ng•hr/mL)† | $C_{max}$ (ng/mL) | $T_{max}$ (hrs) | Trough Conc. (ng/mL) |
|---|---|---|---|---|
| Single Dose 10 mg OxyContin | 100.7 [26.6] | 10.6 [20.1] | 2.7 [44.1] | n.a. |
| 20 mg OxyContin | 207.5 [35.9] | 21.4 [36.6] | 3.2 [57.9] | n.a. |
| 40 mg OxyContin | 423.1 [33.3] | 39.3 [34.0] | 3.1 [77.4] | n.a. |
| Multiple Dose 10 mg OxyContin Tablets q12h | 103.6 [38.6] | 15.1 [31.0] | 3.2 [69.5] | 7.2 [48.1] |
| 5 mg immediate-release q6h | 99.0 [36.2] | 15.5 [28.8] | 1.6 [49.7] | 7.4 [50.9] |

†for single-dose AUC = $AUC_{0-\infty}$; for multiple-dose AUC = $AUC_{0-t}$

*Food Effects*

In contrast to immediate-release formulations, food has no significant effect on the absorption of oxycodone from OxyContin. Oxycodone release from OxyContin tablets is pH independent.

*Distribution*

Following intravenous administration, the volume of distribution (Vss) for oxycodone was 2.6L/kg. Oxycodone binding to plasma protein at 37C° and a pH of 7.4 was about 45%. Once absorbed, oxycodone is distributed to skeletal muscle, liver, intestinal tract, lungs, spleen and brain. Oxycodone has been found in breast milk (see PRECAUTIONS).

*Metabolism*

Oxycodone hydrochloride is extensively metabolized to noroxycodone, oxymorphone, and their glucuronides. The major circulating metabolite is noroxycodone with an AUC ratio of 0.6 relative to that of oxycodone. Noroxycodone is reported to be a considerably weaker analgesic than oxycodone. Oxymorphone, although possessing analgesic activity, is present in the plasma only in low concentrations. The correlation between oxymorphone concentrations and opioid effects was much less than that seen with oxycodone plasma concentrations. The analgesic activity profile of other metabolites is not known at present.

The formation of oxymorphone, but not noroxycodone, is mediated by CYP2D6 and as such its formation can, in theory, be affected by other drugs (see Drug-Drug Interactions).

*Excretion*

Oxycodone and its metabolites are excreted primarily via the kidney. The amounts measured in the urine have been reported as follows: free oxycodone up to 19%; conjugated oxycodone up to 50%; free oxymorphone 0%; conjugated oxymorphone ≤ 14%; both free and conjugated noroxycodone have been found in the urine but not quantified. The total plasma clearance was 0.8 L/min for adults.

*Special Populations*

*Elderly*

The plasma concentrations of oxycodone are only nominally affected by age, being 15% greater in elderly as compared to young subjects. There were no differences in adverse event reporting between young and elderly subjects.

*Gender*

Female subjects have, on average, plasma oxycodone concentrations up to 25% higher than males on a body weight adjusted basis. The reason for this difference is unknown.

*Renal Impairment*

Preliminary data from a study involving patients with mild to severe renal dysfunction (creatinine clearance <60 mL/min) show peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively and AUC values for oxycodone, noroxycodone and oxymorphone 60%, 50% and 40% higher than normal subjects, respectively. This is accompanied by an increase in sedation but not by differences in respiratory rate, pupillary constriction, or several other measures of drug effect. There was an increase in $t_{1/2}$ of elimination for oxycodone of only 1 hour (see PRECAUTIONS).

*Hepatic Impairment*

Preliminary data from a study involving patients with mild to moderate hepatic dysfunction show peak plasma oxycodone and noroxycodone concentrations 50% and 20% higher, respectively, than normal subjects. AUC values are 95% and 65% higher, respectively. Oxymorphone peak plasma concentrations and AUC values are lower by 30% and 40%. These differences are accompanied by increases in some, but not other, drug effects. The $t_{1/2}$ elimination for oxycodone increased by 2.3 hours (see PRECAUTIONS).

*Drug-Drug Interactions* (see PRECAUTIONS)

Oxycodone is metabolized in part via CYP2D6 to oxymorphone which represents less than 15% of the total administered dose. This route of elimination can be blocked by a variety of drugs (e.g., certain cardiovascular drugs and anti-depressants). Patients receiving such drugs concomitantly with OxyContin do not appear to present different therapeutic profiles than other patients.

### CLINICAL TRIALS

OxyContin™ (oxycodone hydrochloride controlled-release) tablets were evaluated in studies involving 713 patients with either cancer or non-cancer pain. All patients receiving OxyContin were dosed q12h. Efficacy comparable to other forms of oral oxycodone was demonstrated in clinical studies using pharmacokinetic, pharmacodynamic and efficacy outcomes. The outcome of these trials indicated: (1) a positive relationship between dose and plasma oxycodone concentration, (2) a positive relationship between plasma oxycodone concentration and analgesia, and (3) an observed peak to trough variation in plasma concentration with OxyContin lying within the observed range established with qid dosing of immediate-release oxycodone in clinical populations at the same total daily dose.

In clinical trials, OxyContin tablets were substituted for a wide variety of analgesics, including acetaminophen (APAP), aspirin (ASA), other non-steroidal anti-inflammatory drugs (NSAIDs), opioid combination products and single-entity opioids, primarily morphine. In cancer patients receiving adequate opioid therapy at baseline, pain intensity scores and acceptability of therapy remained unchanged by transfer to OxyContin. For non-cancer pain patients who had moderate to severe pain at baseline on prn opioid therapy, pain control and acceptability of therapy improved with the introduction of fixed-interval therapy with OxyContin.

*Use in Cancer Pain*

OxyContin was studied in three double-blind, controlled clinical trials involving 341 cancer patients and several open-label trials with therapy durations of over 10 months.

Two, double-blind, controlled clinical studies indicated that OxyContin dosed q12h produced analgesic efficacy equivalent to immediate-release oxycodone dosed qid at the same total daily dose. Peak and trough plasma concentrations attained were similar to those attained with immediate-release oxycodone at equivalent total daily doses. With titration to analgesic effect and proper use of rescue medication, nearly every patient achieved adequate pain control with OxyContin.

In the third study, a double-blind, active-controlled, crossover trial, OxyContin dosed q12h was shown to be equivalent in efficacy and safety to immediate-release oxycodone dosed qid at the same total daily dose. Patients were able to be titrated to an acceptable analgesic effect with either OxyContin or immediate-release oxycodone with both treatments providing stable pain control within 2 days in most patients.

In patients with cancer pain, the total daily OxyContin doses tested ranged from 20 mg to 640 mg per day. The average total daily dose was approximately 105 mg per day.

*Studies in Non-Cancer Pain*

A double-blind, placebo-controlled, fixed-dose, parallel group study was conducted in 133 patients with moderate to severe osteoarthritis pain, who were judged as having inadequate pain control with prn opioids and maximal non-steroidal anti-inflammatory therapy. In this study, 20 mg OxyContin q12h significantly decreased pain and improved quality of life, mood and sleep, relative to placebo. Both dose-concentration and concentration-effect relationships were noted with a minimum effective plasma oxycodone concentration of approximately 5–10 ng/mL.

In a double-blind, active-controlled, crossover study involving 57 patients with low-back pain inadequately controlled with prn opioids and non-opioid therapy, OxyContin administered q12h provided analgesia equivalent to immediate-release oxycodone administered qid. Patients could be titrated to an acceptable analgesic effect with either OxyContin or immediate-release forms of oxycodone.

*Single-Dose Comparison with Standard Therapy*

A single-dose, double-blind, placebo-controlled, post-operative study of 182 patients was conducted utilizing graded doses of OxyContin (10, 20 and 30 mg). Twenty and 30 mg of OxyContin gave equivalent peak analgesic effect compared to two oxycodone 5 mg /acetaminophen 325 mg tablets and to 15 mg immediate-release oxycodone, while the 10 mg dose of OxyContin was intermediate between both the immediate-release and combination products and placebo. The onset of analgesic action with OxyContin occurred within 1 hour in most patients following oral administration.

OxyContin is not recommended pre-operatively (preemptive analgesia) or for the management of pain in the immediate post-operative period (the first 12 to 24 hours following surgery) because the safety or appropriateness of fixed-dose, long-acting opioids in this setting has not been established.

*Other Clinical Trials*

In open-label trials involving approximately 200 patients with cancer-related and non-cancer pain, dosed according to the package insert recommendations, appropriate analgesic effectiveness was noted without regard to age, gender, race, or disease state. There were no unusual drug interactions observed in patients receiving a wide range of medications common in these populations.

For opioid-naive patients, the average total daily dose of OxyContin was approximately 40 mg per day. There was no evidence of oxycodone and metabolite accumulation during 8 months of therapy. For cancer pain patients the average total daily dose was 105 mg (range 20 to 720 mg) per day. There was a significant decrease in acute opioid-related side effects, except for constipation, during the first several weeks of therapy. Development of significant tolerance to analgesia was uncommon.

### INDICATIONS AND USAGE

OxyContin™ tablets are a controlled-release oral formulation of oxycodone hydrochloride indicated for the management of moderate to severe pain where use of an opioid analgesic is appropriate for more than a few days. (See: CLINICAL PHARMACOLOGY; CLINICAL TRIALS).

### CONTRAINDICATIONS

OxyContin™ is contraindicated in patients with known hypersensitivity to oxycodone, or in any situation where opioids are contraindicated. This includes patients with significant respiratory depression (in unmonitored settings or the absence of resuscitative equipment), and patients with acute or severe bronchial asthma or hypercarbia. OxyContin is contraindicated in any patient who has or is suspected of having paralytic ileus.

### WARNINGS

**OxyContin™ (oxycodone hydrochloride controlled-release) TABLETS ARE TO BE SWALLOWED WHOLE, AND ARE NOT TO BE BROKEN, CHEWED OR CRUSHED. TAKING BROKEN, CHEWED OR CRUSHED OxyContin TABLETS COULD LEAD TO THE RAPID RELEASE AND ABSORPTION OF A POTENTIALLY TOXIC DOSE OF OXYCODONE.**

*Respiratory Depression*

Respiratory depression is the chief hazard from all opioid agonist preparations. Respiratory depression occurs most frequently in elderly or debilitated patients, usually following large initial doses in non-tolerant patients, or when opioids are given in conjunction with other agents that depress respiration.

Oxycodone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression. In such patients, even usual therapeutic doses of oxycodone may decrease respiratory drive to the point of apnea. In these patients alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose.

*Head Injury*

The respiratory depressant effects of opioids include carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure, and may be markedly exaggerated in the presence of head injury, intracranial lesions, or other sources of preexisting increased intracranial pressure. Oxycodone produces effects on pupillary response and consciousness which may obscure neurologic signs of further increases in intracranial pressure in patients with head injuries.

*Hypotensive Effect*

OxyContin™, like all opioid analgesics, may cause severe hypotension in an individual whose ability to maintain blood pressure has been compromised by a depleted blood volume, or after concurrent administration with drugs such as phenothiazines or other agents which compromise vasomotor tone. OxyContin may produce orthostatic hypotension in ambulatory patients. OxyContin, like all opioid analgesics, should be administered with caution to patients in circulatory shock, since vasodilation produced by the drug may further reduce cardiac output and blood pressure.

### PRECAUTIONS

*General*

OxyContin™ (oxycodone hydrochloride controlled-release) tablets are intended for use in patients who require oral pain therapy with an opioid agonist of more than a few days duration. As with any opioid analgesic, it is critical to adjust the dosing regimen individually for each patient (see DOSAGE AND ADMINISTRATION).

Selection of patients for treatment with OxyContin should be governed by the same principles that apply to the use of similar controlled-release opioid analgesics (see INDICATIONS AND USAGE). Opioid analgesics given on a fixed-dosage schedule have a narrow therapeutic index in certain patient populations, especially when combined with other drugs, and should be reserved for cases where the benefits of opioid analgesia outweigh the known risks of respiratory depression, altered mental state, and postural hypotension. Physicians should individualize treatment in every case, using non-opioid analgesics, prn opioids and/or combination products, and chronic opioid therapy with drugs such as OxyContin in a progressive plan of pain management such as outlined by the World Health Organization, the Agency for Health Care Policy and Research, and the American Pain Society.

Use of OxyContin is associated with increased potential risks and should be used only with caution in the following conditions: acute alcoholism; adrenocortical insufficiency (e.g., Addison's disease); CNS depression or coma; delirium tremens; debilitated patients; kyphoscoliosis associated with respiratory depression; myxedema or hypothyroidism; prostatic hypertrophy or urethral stricture; severe impairment of hepatic, pulmonary or renal function; and toxic psychosis.

The administration of oxycodone, like all opioid analgesics, may obscure the diagnosis or clinical course in patients with acute abdominal conditions. Oxycodone may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings.

*Interactions with other CNS Depressants*

OxyContin, like all opioid analgesics, should be used with caution and started in a reduced dosage ($\frac{1}{3}$ to $\frac{1}{2}$ of the usual dosage) in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, other tranquilizers and alcohol. Interactive effects resulting in respiratory depression, hypotension, profound sedation or coma may result if these drugs are taken in combination with the usual doses of OxyContin.

*Interactions with Mixed Agonist/Antagonist Opioid Analgesics*

Agonist/antagonist analgesics (i.e., pentazocine, nalbuphine, butorphanol and buprenorphine) should be administered with caution to a patient who has received or is receiving a course of therapy with a pure opioid agonist analgesic such as oxycodone. In this situation, mixed agonist/antagonist analgesics may reduce the analgesic effect of oxycodone and/or may precipitate withdrawal symptoms in these patients.

*Ambulatory Surgery*

OxyContin is not recommended pre-operatively (preemptive analgesia) or for the management of pain in the immediate post-operative period (the first 12 to 24 hours following surgery) for patients not previously taking the drug, because its safety in this setting has not been established.

Patients who are already receiving OxyContin tablets as part of ongoing analgesic therapy may be safely continued on the drug if appropriate dosage adjustments are made considering the procedure, other drugs given and the temporary changes in physiology caused by the surgical intervention (see PRECAUTIONS: Drug-Drug Interactions, and DOSAGE AND ADMINISTRATION).

*Use in Pancreatic/Biliary Tract Disease*

Oxycodone may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis. Opioids like oxycodone may cause increases in the serum amylase level.

*Tolerance and Physical Dependence*

Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Physical dependence is the occurrence of withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist. Physical dependence and tolerance are not unusual during chronic opioid therapy.

Significant tolerance should not occur in most of the patients treated with the lowest doses of oxycodone. It should be expected, however, that a fraction of cancer patients will develop some degree of tolerance and require progressively higher dosages of OxyContin to maintain pain control during chronic treatment. Regardless of whether this occurs as a result of increased pain secondary to disease progression or pharmacological tolerance, dosages can usually be increased safely by adjusting the patient's dose to maintain an acceptable balance between pain relief and side effects. The dosage should be selected according to the patient's individual analgesic response and ability to tolerate side effects. Tolerance to the analgesic effect of opioids is usually paralleled by tolerance to side effects, except for constipation.

Physical dependence results in withdrawal symptoms in patients who abruptly discontinue the drug or may be precipitated through the administration of drugs with opioid antagonist activity (see OVERDOSAGE). If OxyContin is abruptly discontinued in a physically dependent patient, an abstinence syndrome may occur. This is characterized by some or all of the following: restlessness, lacrimation, rhinorrhea, yawning, perspiration, chills, myalgia and mydriasis. Other symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhea, or increased blood pressure, respiratory rate or heart rate.

If signs and symptoms of withdrawal occur, patients should be treated by reinstitution of opioid therapy followed by a gradual, tapered dose reduction of OxyContin combined with symptomatic support (see DOSAGE AND ADMINISTRATION: Cessation of Therapy).

*Information for Patients/Caregivers*

If clinically advisable, patients receiving OxyContin (oxycodone hydrochloride controlled-release) tablets or their caregivers should be given the following information by the physician, nurse, pharmacist or caregiver:

1. Patients should be advised that OxyContin tablets were designed to work properly only if swallowed whole. They may release all their contents at once if broken, chewed or crushed, resulting in a risk of overdose.
2. Patients should be advised to report episodes of breakthrough pain and adverse experiences occurring during therapy. Individualization of dosage is essential to make optimal use of this medication.
3. Patients should be advised not to adjust the dose of OxyContin without consulting the prescribing professional.

4. Patients should be advised that OxyContin may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g., driving, operating heavy machinery).
5. Patients should not combine OxyContin with alcohol or other central nervous system depressants (sleep aids, tranquilizers) except by the orders of the prescribing physician, because additive effects may occur.
6. Women of childbearing potential who become, or are planning to become, pregnant should be advised to consult their physician regarding the effects of analgesics and other drug use during pregnancy on themselves and their unborn child.
7. Patients should be advised that OxyContin is a potential drug of abuse. They should protect it from theft, and it should never be given to anyone other than the individual for whom it was prescribed.
8. Patients should be advised that they may pass empty matrix "ghosts" (tablets) via colostomy or in the stool, and that this is of no concern since the active medication has already been absorbed.
9. Patients should be advised that if they have been receiving treatment with OxyContin for more than a few weeks and cessation of therapy is indicated, it may be appropriate to taper the OxyContin dose, rather than abruptly discontinue it, due to the risk of precipitating withdrawal symptoms. Their physician can provide a dose schedule to accomplish a gradual discontinuation of the medication.

*Laboratory Monitoring*

Due to the broad range of plasma concentrations seen in clinical populations, the varying degrees of pain, and the development of tolerance, plasma oxycodone measurements are usually not helpful in clinical management. Plasma concentrations of the active drug substance may be of value in selected, unusual or complex cases.

*Interactions with Alcohol and Drugs of Abuse*

Oxycodone may be expected to have additive effects when used in conjunction with alcohol, other opioids or illicit drugs which cause central nervous system depression.

*Use in Drug and Alcohol Addiction*

OxyContin is an opioid with no approved use in the management of addictive disorders. Its proper usage in individuals with drug or alcohol dependence, either active or in remission, is for the management of pain requiring opioid analgesia.

*Drug-Drug Interactions*

Opioid analgesics, including OxyContin, may enhance the neuromuscular blocking action of skeletal muscle relaxants and produce an increased degree of respiratory depression.

Oxycodone is metabolized in part to oxymorphone via CYP2D6. While this pathway may be blocked by a variety of drugs (e.g., certain cardiovascular drugs and antidepressants), such blockade has not yet been shown to be of clinical significance with this agent. Clinicians should be aware of this possible interaction, however.

*Use with CNS Depressants*

OxyContin, like all opioid analgesics, should be started at 1/3 to 1/2 of the usual dosage in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, centrally acting anti-emetics, tranquilizers and alcohol because respiratory depression, hypotension and profound sedation or coma may result. No specific interaction between oxycodone and monoamine oxidase inhibitors has been observed, but caution in the use of any opioid in patients taking this class of drugs is appropriate.

*Mutagenicity*

Studies of oxycodone in animals to evaluate its carcinogenic and mutagenic potential have not been conducted owing to the length of clinical experience with the drug substance.

*Pregnancy*

Teratogenic Effects—Category B: Reproduction studies have been performed in rats and rabbits by oral administration at doses up to 8 mg/kg (48 mg/m$^2$) and 125 mg/kg (1375 mg/m$^2$), respectively. These doses are 4 and 60 times a human dose of 120 mg/day (74 mg/m$^2$), based on mg/kg of a 60 kg adult (0.7 and 19 times this human dose based upon mg/m$^2$). The results did not reveal evidence of harm to the fetus due to oxycodone. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nonteratogenic Effects—Neonates whose mothers have been taking oxycodone chronically may exhibit respiratory depression and/or withdrawal symptoms, either at birth and/or in the nursery.

*Labor and Delivery*

OxyContin is not recommended for use in women during and immediately prior to labor and delivery because oral opioids may cause respiratory depression in the newborn.

*Nursing Mothers*

Low concentrations of oxycodone have been detected in breast milk. Withdrawal symptoms can occur in breast-feeding infants when maternal administration of an opioid analgesic is stopped. Ordinarily, nursing should not be undertaken while a patient is receiving OxyContin since oxycodone may be excreted in the milk.

*Pediatric Use*

Safety and effectiveness in pediatric patients below the age of 18 have not been established with this dosage form of oxycodone. However, oxycodone has been used extensively in the pediatric population in other dosage forms, as have the excipients used in this formulation. No specific increased risk is expected from the use of this form of oxycodone in pediatric patients old enough to safely take tablets if dosing is adjusted for the patient's weight (see DOSAGE AND ADMINISTRATION). **It must be remembered that OxyContin tablets cannot be crushed or divided for administration.**

*Geriatric Use*

In controlled pharmacokinetic studies in elderly subjects (greater than 65 years) the clearance of oxycodone appeared to be slightly reduced. Compared to young adults, the plasma concentrations of oxycodone were increased approximately 15%. In clinical trials with appropriate initiation of therapy and dose titration, no untoward or unexpected side effects were seen based on age, and the usual doses and dosing intervals are appropriate for the geriatric patient. As with all opioids, the starting dose should be reduced to 1/3 to 1/2 of the usual dosage in debilitated, non-tolerant patients.

*Hepatic Impairment*

A study of OxyContin in patients with hepatic impairment indicates greater plasma concentrations than those with normal function. The initiation of therapy at 1/3 to 1/2 the usual doses and careful dose titration is warranted.

*Renal Impairment*

In patients with renal impairment, as evidenced by decreased creatinine clearance (< 60 mL/min.), the concentrations of oxycodone in the plasma are approximately 50% higher than in subjects with normal renal function. Dose initiation should follow a conservative approach. Dosages should be adjusted according to the clinical situation.

*Gender Differences*

In pharmacokinetic studies, opioid-naive females demonstrate up to 25% higher average plasma concentrations and greater frequency of typical opioid adverse events than males, even after adjustment for body weight. The clinical relevance of a difference of this magnitude is low for a drug intended for chronic usage at individualized dosages, and there was no male/female difference detected for efficacy or adverse events in clinical trials.

## ADVERSE REACTIONS

Serious adverse reactions which may be associated with OxyContin™ (oxycodone hydrochloride controlled-release) tablet therapy in clinical use are those observed with other opioid analgesics, including: respiratory depression, apnea, respiratory arrest, and (to an even lesser degree) circulatory depression, hypotension or shock (see OVERDOSE).

The non-serious adverse events seen on initiation of therapy with OxyContin are typical opioid side effects. These events are dose-dependent, and their frequency depends upon the dose, the clinical setting, the patient's level of opioid tolerance, and host factors specific to the individual. They should be expected and managed as a part of opioid analgesia. The most frequent (>5%) include constipation, nausea, somnolence, dizziness, vomiting, pruritus, headache, dry mouth, sweating and asthenia.

In many cases the frequency of these events during initiation of therapy may be minimized by careful individualization of starting dosage, slow titration, and the avoidance of large swings in the plasma concentrations of the opioid. Many of these adverse events will cease or decrease in intensity as OxyContin therapy is continued and some degree of tolerance is developed.

In clinical trials comparing OxyContin with immediate-release oxycodone and placebo, the most common adverse events (>5%) reported by patients (pts) at least once during therapy were:

**Table 2**

| | OxyContin n=227 # pts (%) | | Immediate-Release n=225 # pts (%) | | Placebo n=45 # pts (%) | |
|---|---|---|---|---|---|---|
| Constipation | 52 | (23) | 58 | (26) | 3 | (7) |
| Nausea | 52 | (23) | 60 | (27) | 5 | (11) |
| Somnolence | 52 | (23) | 55 | (24) | 2 | (4) |
| Dizziness | 29 | (13) | 35 | (16) | 4 | (9) |
| Pruritus | 29 | (13) | 28 | (12) | 1 | (2) |
| Vomiting | 27 | (12) | 31 | (14) | 3 | (7) |
| Headache | 17 | (7) | 19 | (8) | 3 | (7) |
| Dry Mouth | 13 | (6) | 15 | (7) | 1 | (2) |
| Asthenia | 13 | (6) | 16 | (7) | — | — |
| Sweating | 12 | (5) | 13 | (6) | 1 | (2) |

The following adverse experiences were reported in OxyContin treated patients with an incidence between 1% and 5%. In descending order of frequency they were anorexia, nervousness, insomnia, fever, confusion, diarrhea, abdominal pain, dyspepsia, rash, anxiety, euphoria, dyspnea, postural hypotension, chills, twitching, gastritis, abnormal dreams, thought abnormalities, and hiccups.

The following adverse reactions occurred in less than 1% of patients involved in clinical trials:

*General:* accidental injury, chest pain, facial edema, malaise, neck pain, pain

*Cardiovascular:* migraine, syncope, vasodilation, ST depression

*Digestive:* dysphagia, eructation, flatulence, gastrointestinal disorder, increased appetite, nausea and vomiting, stomatitis

*Hemic and Lymphatic:* lymphadenopathy

*Metabolic and Nutritional:* dehydration, edema, peripheral edema, thirst

*Nervous:* abnormal gait, agitation, amnesia, depersonalization, depression, emotional lability, hallucination, hyperkinesia, hypesthesia, hypotonia, malaise, paresthesia, speech disorder, stupor, tinnitus, tremor, vertigo, withdrawal syndrome

*Respiratory:* cough increased, pharyngitis, voice alteration

*Skin:* dry skin, exfoliative dermatitis

*Special Senses:* abnormal vision, taste perversion

*Urogenital:* dysuria, hematuria, impotence, polyuria, urinary retention, urination impaired

## DRUG ABUSE AND DEPENDENCE (Addiction)

OxyContin™ is a mu-agonist opioid with an abuse liability similar to morphine and is a Schedule II controlled substance. Oxycodone products are common targets for both drug abusers and drug addicts. Delayed absorption, as provided by OxyContin tablets, is believed to reduce the abuse liability of a drug.

Drug addiction (drug dependence, psychological dependence) is characterized by a preoccupation with the procurement, hoarding, and abuse of drugs for non-medicinal purposes. Drug dependence is treatable, utilizing a multi-disciplinary approach, but relapse is common. Iatrogenic "addiction" to opioids legitimately used in the management of pain is very rare. "Drug seeking" behavior is very common to addicts. Tolerance and physical dependence in pain patients are *not* signs of psychological dependence. Preoccupation with achieving adequate pain relief can be appropriate behavior in a patient with poor pain control. Most chronic pain patients limit their intake of opioids to achieve a balance between the benefits of the drug and dose-limiting side effects.

Physicians should be aware that psychological dependence may not be accompanied by concurrent tolerance and symptoms of physical dependence in all addicts. In addition, abuse of opioids can occur in the absence of true psychological dependence and is characterized by misuse for non-medical purposes, often in combination with other psychoactive substances.

OxyContin consists of a dual-polymer matrix, intended for oral use only. Parenteral venous injection of the tablet constituents, especially talc, can be expected to result in local tissue necrosis and pulmonary granulomas.

## OVERDOSAGE

Acute overdosage with oxycodone can be manifested by respiratory depression, somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, constricted pupils, bradycardia, hypotension, and death.

In the treatment of oxycodone overdosage, primary attention should be given to the re-establishment of a patent airway and institution of assisted or controlled ventilation. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

The pure opioid antagonists such as naloxone or nalmefene are specific antidotes against respiratory depression from opioid overdose. Opioid antagonists should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose. They should be administered cautiously to persons who are known, or suspected to be, physically dependent on any opioid agonist including OxyContin™. In such cases, an abrupt or complete reversal of opioid effects may precipitate an acute abstinence syndrome. The severity of the withdrawal syndrome produced will depend on the degree of physical dependence and the dose of the antagonist administered. Please see the prescribing information for the specific opioid antagonist for details of their proper use.

## DOSAGE AND ADMINISTRATION

*General Principles*

**OxyContin™ (oxycodone hydrochloride controlled-release) TABLETS ARE TO BE SWALLOWED WHOLE, AND ARE NOT TO BE BROKEN, CHEWED OR CRUSHED. TAKING BROKEN, CHEWED OR CRUSHED OxyContin TABLETS COULD LEAD TO THE RAPID RELEASE AND ABSORPTION OF A POTENTIALLY TOXIC DOSE OF OXYCODONE.**

In treating pain it is vital to assess the patient regularly and systematically. Therapy should also be regularly reviewed and adjusted based upon the patient's own reports of pain and side effects and the health professional's clinical judgment.

OxyContin is intended for the management of moderate to severe pain in patients who require treatment with an oral opioid analgesic for more than a few days. The controlled-release nature of the formulation allows it to be effectively administered every 12 hours. (See CLINICAL PHARMACOLOGY; PHARMACOKINETICS AND METABOLISM.) While symmetric (same dose AM and PM), around-the-clock, q12h dosing is appropriate for the majority of patients, some patients may benefit from asymmetric (different dose given in AM than in PM) dosing, tailored to their pain pattern. It is usually appropriate to treat a patient with only one opioid for around-the-clock therapy.

*Initiation of Therapy*

It is critical to initiate the dosing regimen for each patient individually, taking into account the patient's prior opioid and non-opioid analgesic treatment. Attention should be given to:

(1) the general condition and medical status of the patient

(2) the daily dose, potency and kind of the analgesic(s) the patient has been taking

(3) the reliability of the conversion estimate used to calculate the dose of oxycodone

(4) the patient's opioid exposure and opioid tolerance (if any)

(5) the balance between pain control and adverse experiences

Care should be taken to use low initial doses of OxyContin in patients who are not already opioid tolerant, especially those who are receiving concurrent treatment with muscle relaxants, sedatives, or other CNS active medications (see PRECAUTIONS: Drug-Drug Interactions).

*Patients Not Already Taking Opioids (opioid naive)*

Clinical trials have shown that patients may initiate analgesic therapy with OxyContin. A reasonable starting dose for most patients who are opioid naive is 10 mg q12h. If a non-opioid analgesic [(aspirin (ASA), acetaminophen (APAP) or a non-steroidal anti-inflammatory (NSAID)] is being provided, it may be continued. If the current non-opioid is discontinued, early upward dose titration may be necessary.

*Conversion from Fixed-Ratio Opioid/APAP, ASA, or NSAID Combination Drugs*

Patients who are taking 1 to 5 tablets/capsules/caplets per day of a regular strength fixed-combination opioid/non-opioid should be started on 10 to 20 mg OxyContin q12h. For patients taking 6 to 9 tablets/capsules/ caplets, a starting dose of 20 to 30 mg q12h is suggested. For those taking 10 to 12 tablets, caplets or capsules a day, 30 to 40 mg q12h should be considered. The non-opioid may be continued as a separate drug. Alternatively, a different non-opioid analgesic may be selected. If the decision is made to discontinue the non-opioid analgesic, consideration should be given to early upward titration.

*Patients Currently on Opioid Therapy*

If a patient has been receiving opioid-containing medications prior to OxyContin therapy, the total daily (24-hour) dose of the other opioids should be determined.

1. Using standard conversion ratio estimates (see Table 3 below), multiply the mg/day of the previous opioids by the appropriate multiplication factors to obtain the equivalent total daily dose of oral oxycodone.
2. Divide this 24-hour oxycodone dose in half to obtain the twice a day (q12h) dose of OxyContin.
3. Round down to a dose which is appropriate for the tablet strengths available (10, 20, and 40 mg tablets).
4. Discontinue all other around-the-clock opioid drugs when OxyContin therapy is initiated.

No fixed conversion ratio is likely to be satisfactory in all patients, especially patients receiving large opioid doses. The recommended doses shown in Table 3 are only a starting point, and close observation and frequent titration are indicated until patients are stable on the new therapy.

**Table 3**

*Multiplication Factors for Converting the Daily Dose of Prior Opioids to the Daily Dose of Oral Oxycodone**

(Mg/Day Prior Opioid x Factor = Mg/Day Oral Oxycodone)

| | Oral Prior Opioid | Parenteral Prior Opioid |
|---|---|---|
| Oxycodone | 1 | — |
| Codeine | 0.15 | — |
| Fentanyl TTS | SEE BELOW | SEE BELOW |
| Hydrocodone | 0.9 | — |
| Hydromorphone | 4 | 20 |
| Levorphanol | 7.5 | 15 |
| Meperidine | 0.1 | 0.4 |
| Methadone | 1.5 | 3 |
| Morphine | 0.5 | 3 |

*To be used only for conversion to oral oxycodone. For patients receiving high-dose parenteral opioids, a more conservative conversion is warranted. For example, for high-dose parenteral morphine, use 1.5 instead of 3 as a multiplication factor.

In all cases, supplemental analgesia (see below) should be made available in the form of immediate-release oral oxycodone or another suitable short-acting analgesic.

OxyContin can be safely used concomitantly with usual doses of non-opioid analgesics and analgesic adjuvants, provided care is taken to select a proper initial dose (see PRECAUTIONS).

*Conversion from Transdermal Fentanyl to OxyContin*

Eighteen hours following the removal of the transdermal fentanyl patch, OxyContin treatment can be initiated. Although there has been no systematic assessment of such conversion, a conservative oxycodone dose, approximately 10 mg q12h of OxyContin, should be initially substituted for each 25 μg/hr fentanyl transdermal patch. The patient should be followed closely for early titration as there is very limited clinical experience with this conversion.

*Managing Expected Opioid Adverse Experiences*

Most patients receiving opioids, especially those who are opioid naive, will experience side effects. Frequently the side effects from OxyContin are transient, but may require evaluation and management. Adverse events such as constipation should be anticipated and treated aggressively and prophylactically with a stimulant laxative and/or stool softener. Patients do not usually become tolerant to the constipating effects of opioids.

Other opioid-related side effects such as sedation and nausea are usually self-limited and often do not persist beyond the first few days. If nausea persists and is unacceptable to the patient, treatment with anti-emetics or other modalities may relieve these symptoms and should be considered.

Patients receiving OxyContin may pass an intact matrix "ghost" in the stool or via colostomy. These ghosts contain little or no residual oxycodone and are of no clinical consequence.

*Individualization of Dosage*

Once therapy is initiated, pain relief and other opioid effects should be frequently assessed. Patients should be titrated to adequate effect (generally mild or no pain with the regular use of no more than two doses of supplemental analgesia per 24 hours). Rescue medication should be available (see: Supplemental Analgesia). Because steady-state plasma concentrations are approximated within 24 to 36 hours, dosage adjustment may be carried out every 1 to 2 days. It is most appropriate to increase the q12h dose, not the dosing frequency. There is no clinical information on dosing intervals shorter than q12h. As a guideline, except for the increase from 10 mg to 20 mg q12h, the total daily oxycodone dose usually can be increased by 25% to 50% of the current dose at each increase.

If signs of excessive opioid-related adverse experiences are observed, the next dose may be reduced. If this adjustment leads to inadequate analgesia, a supplemental dose of immediate-release oxycodone may be given. Alternatively, non-opioid analgesic adjuvants may be employed. Dose adjustments should be made to obtain an appropriate balance between pain relief and opioid-related adverse experiences.

If significant adverse events occur before the therapeutic goal of mild or no pain is achieved, the events should be treated aggressively. Once adverse events are under control, upward titration should continue to an acceptable level of pain control.

During periods of changing analgesic requirements, including initial titration, frequent contact is recommended between physician, other members of the health-care team, the patient and the caregiver/family.

*Supplemental Analgesia*

Most cancer patients given around-the-clock therapy with controlled-release opioids will need to have immediate-release medication available for "rescue" from breakthrough pain or to prevent pain that occurs predictably during certain patient activities (incident pain).

Rescue medication can be immediate-release oxycodone, either alone or in combination with acetaminophen, aspirin or other NSAIDs as a supplemental analgesic. The supplemental analgesic should be prescribed at 1/4 to 1/3 of the 12-hour OxyContin dose as shown in Table 4. The rescue medication is dosed as needed for breakthrough pain and administered one hour before anticipated incident pain. If more than two doses of rescue medication are needed within 24 hours, the dose of OxyContin should be titrated upward. Caregivers and patients using prn rescue analgesia in combination with around-the-clock opioids should be advised to report incidents of breakthrough pain to the physician managing the patient's analgesia (see Information for Patients/Caregivers).

**Table 4**

*Table of Appropriate Supplemental Analgesia*

| OxyContin q12h Dose (mg) | prn Rescue Dose immediate-release oxycodone (mg) |
|---|---|
| 10 (1×10 mg) | 5 |
| 20 (2×10 mg) | 5 |
| 30 (3×10 mg) | 10 |
| 40 (2×20 mg) | 10 |
| 60 (3×20 mg) | 15 |
| 80 (2×40 mg) | 20 |
| 120 (3×40 mg) | 30 |

*Maintenance of Therapy*

The intent of the titration period is to establish a patient-specific q12h dose that will maintain adequate analgesia with acceptable side effects for as long as pain relief is necessary. Should pain recur then the dose can be incrementally increased to re-establish pain control. The method of therapy adjustment outlined above should be employed to re-establish pain control.

During chronic therapy, especially for non-cancer pain syndromes, the continued need for around-the-clock opioid therapy should be reassessed periodically (e.g., every 6 to 12 months) as appropriate.

*Cessation of Therapy*

When the patient no longer requires therapy with OxyContin tablets, patients receiving doses of 20–60 mg/day can usually have the therapy stopped abruptly without incident. However, higher doses should be tapered over several days to prevent signs and symptoms of withdrawal in the physically dependent patient. The daily dose should be reduced by approximately 50% for the first two days and then reduced by 25% every two days thereafter until the total dose reaches the dose recommended for opioid naive patients (10 or 20 mg q12h). Therapy can then be discontinued.

If signs of withdrawal appear, tapering should be stopped. The dose should be slightly increased until the signs and symptoms of opioid withdrawal disappear. Tapering should then begin again but with longer periods of time between each dose reduction.

*Conversion from OxyContin to Parenteral Opioids*

To avoid overdose, conservative dose conversion ratios should be followed. Initiate treatment with about 50% of the estimated equianalgesic daily dose of parenteral opioid divided into suitable individual doses based on the appropriate dosing interval, and titrate based upon the patient's response.

## SAFETY AND HANDLING

OxyContin™ (oxycodone hydrochloride controlled-release) tablets are solid dosage forms that pose no known health risk to health-care providers beyond that of any controlled substance. As with all such drugs, care should be taken to prevent diversion or abuse by proper handling.

## HOW SUPPLIED

OxyContin™ (oxycodone hydrochloride controlled-release) 10 mg tablets are round, unscored, white-colored, convex tablets bearing the symbol OC on one side and 10 on the other. They are supplied as follows:

**NDC** 59011-100-10: child-resistant closure, opaque plastic bottles of 100

OxyContin (oxycodone hydrochloride controlled-release) 20 mg tablets are round, unscored, pink-colored, convex tablets bearing the symbol OC on one side and 20 on the other. They are supplied as follows:

**NDC** 59011-103-10: child-resistant closure, opaque plastic bottles of 100

OxyContin (oxycodone hydrochloride controlled-release) 40 mg tablets are round, unscored, yellow-colored, convex tablets bearing the symbol OC on one side and 40 on the other. They are supplied as follows:

**NDC** 59011-105-10: child-resistant closure, opaque plastic bottles of 100

Store tablets at controlled room temperature 15–30°C (59–86°F).

Dispense in tight, light-resistant container.

## CAUTION

**DEA Order Form Required.**

**Federal law prohibits dispensing without prescription.**

Manufactured by The PF Laboratories, Inc.
Totowa, N.J. 07512

Distributed by Purdue Pharma L.P.
Norwalk, CT 06850-3590



U.S. Patent Numbers 4,861,598; 4,970,075; and 5,266,331

December 5, 1995

A4909-811

# Exhibit 3

Networking that works

# Teamlink

VOLUME 11, NUMBER 1 THE PURDUE FREDERICK COMPANY WINTER 1996

# OxyContin™: The Most Significant Launch in Purdue History!

For millennia, humans knew that great changes in the fortunes of civilizations and enterprises are heralded by cataclysms in geology and weather.

Eclipses, earthquakes, volcanoes, hurricanes, and blizzards have each preceded such changes, and each upheaval has had its significance and meaning.

Soothsayers and wise men, shamans and high priestesses, each have a claim on the capacity to interpret such phenomena for the rest of us and advise us about how we should now align ourselves for the coming of the New Age.

The Blizzard of '96, coming less than four years before the change of the millennium, is without doubt an omen of change.

This unexpected surge of snow, this untimely tempest threw a wrench into the flawless planning that Jim, Ron, and dozens of others had made to bring us all together here on Sunday evening. Unfortunately Michael, Paul, Robert and I were not with you on Sunday, nor on Monday nor today. Even now Paul and Robert are absent.

But the reason for our absence is not what you imagined or been told. "They are stuck in Connecticut because the East Coast is shut down," you must have believed. **Balderdash! Poppycock! Twaddle! Babble! Nonsense!** This was just a subtle subterfuge to deflect your brilliant powers of deduction from discerning the truth, which is, that we were on a final and unexpected mission to enhance the launch of OxyContin Tablets.

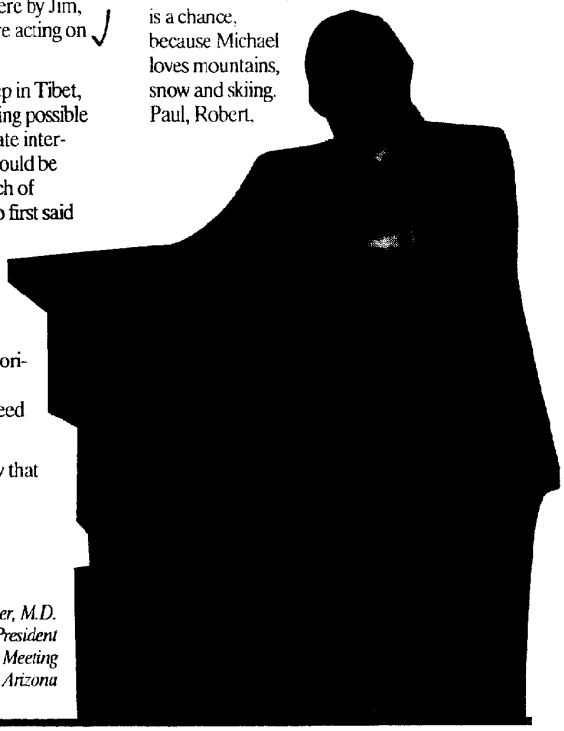
Michael and I were late (and Paul and Robert are missing) not because transportation was snarled and airports were closed. We apologize for the disinformation spread here by Jim, Ron, Mark and others, but they were acting on Michael's orders.

We were high in the Himalayas, deep in Tibet, to learn from the Wise One everything possible about the meaning of this intemperate interruption of our plans and what we should be doing to take advantage of the launch of OxyContin Tablets. It was Paul who first said that it was imprudent to depend upon our own powers of prognostication. "Let's go where the knowledge is," suggested Paul. We all wanted to be sure that we were bringing you the most authoritative information about the significance of the Blizzard of '96. "We need an expert," said Paul conclusively.

"Forget it, guys," I said. "You know that Michael thinks that consultants are vermin, and that that they borrow your watch to tell you the time."

"There is an alternative to McKinsey," said Robert Reder. "I know a Wise One in the mountains of Tibet."

I ventured. "Well, there is a chance, because Michael loves mountains, snow and skiing. Paul, Robert,



*Richard Sackler, M.D.*
*Senior Vice President*
*At the podium at the National Launch Meeting*
*The Wigwam, Arizona*

*continued next page*

why don't you call Michael and invite him for some fun and snow. That should sink the hook in really deeply."

IT WORKED! After an exhausting and hair raising trip, we were deep in the Himalayas, high on the flank of Anapurna, one of the most famous mountains in the Himalayas, inside a monastery inhabited by the Wise One.

"Oh Wise One," we incanted. "What is the meaning of all this snow where little or no snow should go?"

The incense smoke was dense, the torrid atmosphere was electric, as the Wise One closed his eyes in a trance.

"Are you poets or are you members of the Greatest Sales Force On Earth?" he demanded in a stentorian staccato which startled us into instant attention.

"We are salesmen," we chanted in unison.

"That's a relief," replied the Wise One, "because as poets you're not too good, but as salesmen, you are a Company of the Best."

The Wise One sank again into impenetrable torpor. "I now see," he cryptically whispered, as the smoke had grown so thick that I could see nothing whatsoever, and I was in the midst of taking off my contacts for the second time believing that I had reversed the left and right lenses and put them on inside out as well.

"The significance of the Blizzard of '96 is that the launch of OxyContin Tablets will be followed by a blizzard of prescriptions that will bury the competition. The prescription blizzard will be so deep, dense and white that you will never see their White Flag. Commerce in competitive products will come to a halt; on advice of the Law Department, let me amend that. Commerce in competitive products will come to a virtual halt."

He continued. "You will revolutionize the treatment both of chronic pain of cancer and of non-malignant, painful conditions as well. And OxyContin Tablets will be a revolutionary product, because with its rapid time of onset, titration with each dose and one day to steady state, it will be the first controlled release drug to beat immediate release competitors at their own game, the treatment of acute conditions."

"Is that all?" we chorused in unison. After all, we had traveled 12,000 miles and climbed cliffs defying the laws of gravity and our acrophobia. "You can tell us no more than this? We knew that before we came here. We wanted you to give us additional knowledge so that we could be even more successful."

Paul added, "We knew of its potential from the most comprehensive clinical program ever conducted for any analgesic drug anywhere."

Michael's voice, building in volume, boomed, "And we had the most comprehensive market research ever developed for any launch at any time. It told us that 90% of physicians have a high level of interest in OxyContin Tablets, and that most of them intend being early prescribers, in fact, as soon as OxyContin Tablets are available. We knew all of this before we came here, this, and a lot more."

*OxyContin Tablets is the most important product launch in the company's history, and like the Blizzard of '96, will become a part of our common and individual history. In the years to come we will look back on this week as the beginning of a New Era for our business and for ourselves.*

The Wise One looked startled. But he recovered his composure in an instant and said, "Well, Big Red, I have a question for you," he taunted. "If you knew all this before you came here, why did you bother coming here in the first place?"

We answered as one. "We came here because there is absolutely nothing that is ethical and legal that we won't do to make the Greatest Sales force On Earth even more successful!"

And that's the truth.

The trip back was easier than we expected. Skiing down from the High Himalayas was thrilling for Michael and me; unfortunately, Paul and Robert only cross country ski, and they are still plugging along somewhere deep in the snow.

OxyContin Tablets is the most important product launch in the company's history, and like the Blizzard of '96, will become a part of our common and individual history. In the years to come we will look back on this week as the beginning of a New Era for our business and for ourselves.

We'll leave the slippery slopes of this anecdote before I really slide into an abysmal metaphor that I can't ski out of.

PAUSE

Seriously, the launch of OxyContin Tablet is the most important product launch in the history of the company. It marks the beginning of a new history for Purdue, a history of more innovative products, more frequently launched, with more skills and resources applied than ever before. I hope that it is of interest to you to know something of the other things that make the development of OxyContin Tablets uniquely important.

Allow me to cite some of the dozens of things in the process that are importantly different and prophetic because they point to a new aggressiveness of management of our team.

The development and launching of OxyContin Tablets is the first time that we have chosen to obsolete our own product, and we have done it before the competition has slowed our growth of sales.

The writing of the package insert was one of the earliest parts of the project. The first draft was penned by Bob Kaiko and Robert Reder almost three years before the NDA was filed. It was thereafter revised more than 30 times. This unprecedented team effort of medical researchers, scientific communications experts, sales and marketing personnel and others was an enormous commitment of time and energy to the project.

Whenever you read any part of the package insert, you should remember the hundreds of hours of work that went into each section, paragraph, sometimes each phrase and word. This was extremely demanding work, but from the first to the last, I observed that the team working on this never lost their temper, never ceased to support the effort and each other, and every time made the label better, stronger, a more potent selling instrument.

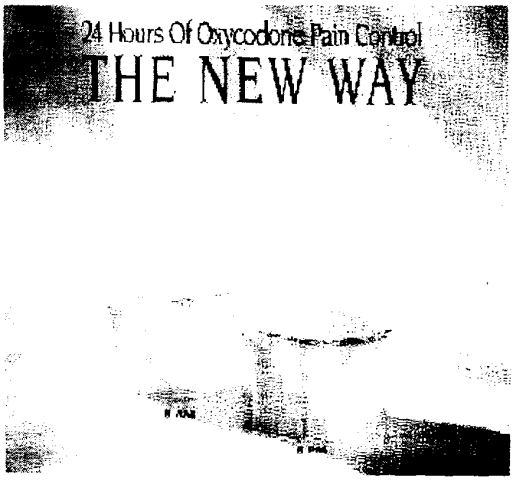
And we have the most powerful selling package insert in the category and in the industry.

*continued on page 8*

# Sales & Marketing Update

*Jim Lang*

As I am writing this article, we are at the very early stages of the OxyContin™ launch. Many representatives have started very quickly by getting the required number of stores stocked in order to obtain certification to begin presenting the product to physicians and nurses. The initial prescription reports are most encouraging; we are well ahead of any previous product launch performance. What is particularly striking is that prior to representatives being certified, we are beginning to see significant prescriptions. Certainly, that bodes well for the product, and validates the excitement we have observed from physicians and nurses for the product.




I have been responsible for managing sales representatives for approximately 25 years. It never ceases to amaze me to see the representative/manager excitement and confidence created by the anticipated success of a new product. With some representatives, however, this does not translate into the anticipated results. Some of the key factors contributing to this problem are as follows:

- The product is perceived as being so good it will sell itself.
- Representatives have been lulled into thinking they have superior sales skills because of the success they have experienced with products such as MS Contin®, Uniphyl®, and Betadine®.
- Representatives fail to take into consideration the powerful influence that old habits have on physician prescribing patterns.
- During the initial stages of a launch, representatives attempt to sell everyone in the territory on the significance of the product, not recognizing that call frequency is equally important.
- With new products, some representatives have a tendency to "tell" rather than sell.
- Representatives fail to uncover the special needs of the physician during the sales presentation. Representatives may thus "blow away" the physician with a multitude of facts, instead of giving the physician the specific information she/he needs to feel comfortable in prescribing the product.

Ladies and gentlemen, selling an exciting new product such as OxyContin requires high levels of sales strategy development skills and presentation skills. Calling on a physician who has switched from MS Contin to Duragesic® or Oramorph SR® also requires this. During the launch of OxyContin, please evaluate the quality and the effectiveness of your sales presentations based on your most successful sales presentations given to physicians who have switched to MS Contin, or to any of our other products, from a competitor's product. If, at the end of an OxyContin call, you can say, "I got that client," chances are you probably did achieve success.

Demand of yourself the best you can give. Now is the time to put in those extra hours at the end of the day or on weekends, honing your product knowledge, your presentation skills, and territory management abilities to ensure you maximize your efforts to achieve personal success.

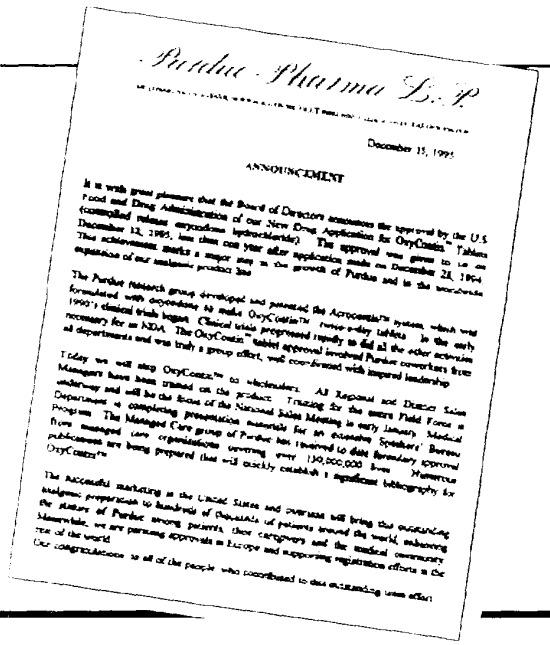
We are looking forward to a fantastic OxyContin success during 1996. We are also looking forward to a fantastic sales increase during 1996 to assist us in moving quickly toward our goal of achieving $1 billion in annual sales. Good selling! ■

*Mark Alfonso*

By the time you receive this issue of TeamLink, we will be well on our way towards making OxyContin™ a major success. But that is only the beginning. The sales forecast for the rest of our product portfolio is $240,750,000. To meet that forecast the Marketing Department is doing all it can to help you maintain and increase sales for all our products.

We have added a Promotional Writer to our Creative Services group. We continue to increase our consumer advertising for OTC products, in addition to creating promotions targeted to specific national accounts. Our antiseptic group is working on a test market for a line extension. We are expanding our Uniphyl® campaign to the COPD market, while continuing to emphasize the anti-inflammatory properties of theophylline and the benefits that Uniphyl provides to the asthma patient. Finally, we are creating promotional material that will help protect MS Contin® while we build OxyContin sales.

On behalf of our Product Managers, Creative Services and the Market Research team, I wish you great success. Be assured that we are ready to support your efforts in every possible way. ■


Purdue Pharma L.P.

December 15, 1995

ANNOUNCEMENT

It is with great pleasure that the Board of Directors announces the approval by the U.S. Food and Drug Administration of our New Drug Application for OxyContin™ Tablets (controlled release oxycodone hydrochloride). The approval was given to us on December 13, 1995, less than one year after application made on December 28, 1994. This achievement marks a major step in the growth of Purdue and in the successful expansion of our analgesic product line.

The Purdue research group developed and patented the Acroscentric® system, which was formulated with oxycodone to make OxyContin™ twice-a-day tablets. In the early 1990's clinical trials began. Clinical trials progressed rapidly to fulfill all the other requirements necessary for an NDA. The OxyContin™ tablet approval involved Purdue researchers from all departments and was truly a group effort, well coordinated with inspired leadership.

Today we will ship OxyContin™ to wholesalers. All Regional and District Sales Managers have been trained on the product. Training for the entire Field Force is underway and will be the focus of the National Sales Meeting in early January. Medical Department is completing presentation materials for an extensive Speakers' Bureau Program. The Managed Care group of Purdue has journeyed to their formulary approval from managed care organizations covering over 130,000,000 lives. Numerous publications are being prepared that will quickly establish a significant bibliography for OxyContin™.

The successful marketing in the United States and overseas will bring the outstanding analgesic properties to hundreds of thousands of patients around the world, enhancing the stature of Purdue among patients, their caregivers and the medical community. Meanwhile, we are pursuing approvals in Europe and supporting registration efforts in the rest of the world.

Our congratulations to all of the people who contributed to this outstanding team effort.

# Awaken the Sleeping Giant!

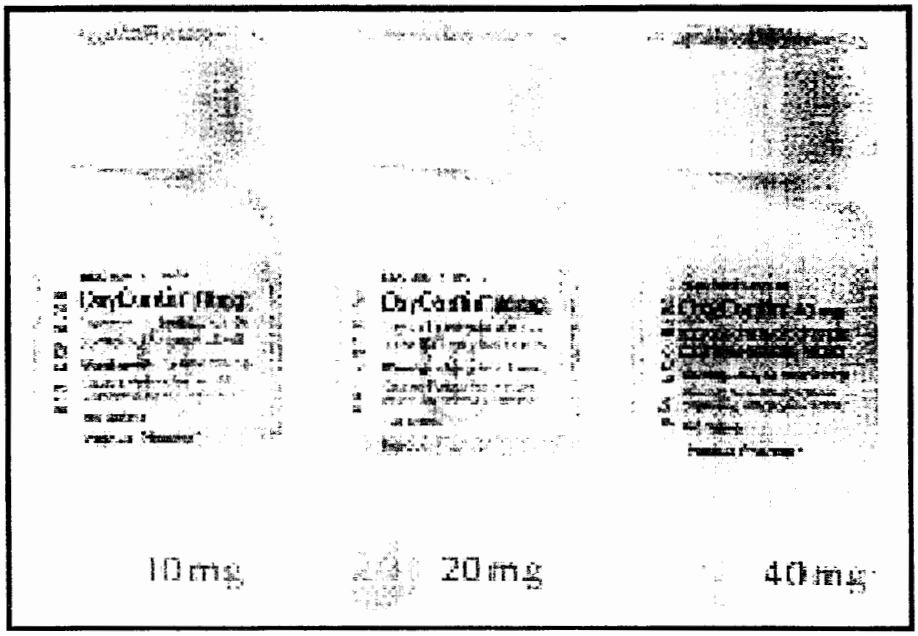
*Mike Innaurato*

You have set off the alarm clock and "the sleeping giant" is up and running. At the time of this writing, OxyContin™ Tablets factory sales have exceeded $8.2 million dollars. That's almost one-third of this year's forecast. All indications are that we have a potential blockbuster product on our hands!

OxyContin is the one that we plan to start and stay with. Our strategy involves convincing health care professionals to start with OxyContin as soon as patients with moderate to severe pain require opioid therapy for more than a few days. It is also the one to stay with by titrating the dose, thereby eliminating or delaying the need for other long-acting products. This strategy more than doubles the market potential for OxyContin compared to MS Contin™, which increases your potential for greater bonus earnings. As you learned at the National Sales Meeting, it is critical that we employ this defensive marketing strategy of obtaining all new patients on OxyContin and not MS Contin. This will allow us to maintain our sales volume before our competitors try to steal it away from us!

By now, all of you have received our three-page visual aid which was approved by FDA in early February. We are still awaiting approval for all other promotional materials at the time of this writing. Journal advertising began during the first week of March in such journals as *Medical Economics*, *New England Journal of Medicine*, *American Medical News*, *Journal of Clinical Oncology*, and many others. The journal ad is exactly the same as the three-page visual that you are using to sell health care professionals. This will ensure a consistent message and strong brand identity with our "cups" campaign.

Our extensive direct mail campaign will begin in March and will continue through the fourth quarter. A one-page launch announcement letter will be the first mailing that our target audiences will receive. Following this announcement, doctors and nurses will receive numerous mailings every three weeks. As soon as they are approved by the FDA, letters will be available through the Precise System as a follow- up to your sales call. In addition, we will attend 14 different conventions this year with the new OxyContin exhibit structure and medical symposia are being planned for most of these meetings.




Many new and exciting programs are under development for the second and third quarter action plans. You will be receiving new OxyContin selling tools such as reprint carriers, an insert-vice slide module, a formulary kit, an OxyIR™ file card, as well as OxyContin reminder items such as prescription pad holders, phone message pads, post-it notes, pens, etc.

As you can see, we have big plans in store for OxyContin and you should too! Now is the time to cash in on the bonus earnings that OxyContin will provide. You have the knowledge, you have the tools, all you need is the hunger to make it to Toppers. Good luck and good selling! ■

(need to fill space??)

# OxyContin™ Training

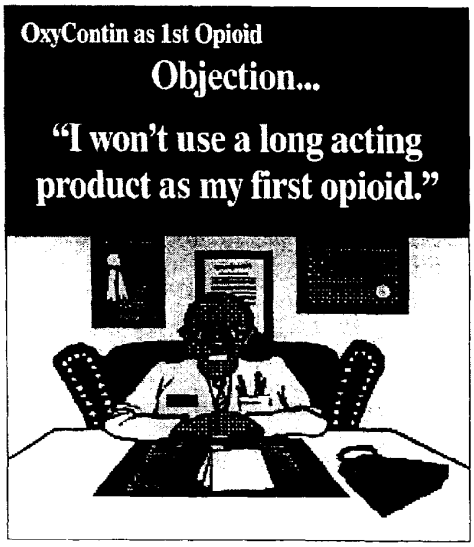
*Jerry Pizzola*

Training and Development has been working diligently to assure that your training needs are being met. The *OxyContin™ Tablets Training and Development Program Binder* has evoked some interesting views on our targeted patient's profiles. Chapter 8 will contribute new target rationales and added selling phrases. The National Meeting workshops and quizzes are now history. A New Hire Phase I Training Program has been amended to include OxyContin. You have just practiced "Proving and Explaining" to statements made by your physicians regarding OxyContin. So what's in store to support your future selling efforts regarding OxyContin Tablets?

Here are some examples of what to expect:

1. A *Teamlink Audio Magazine* devoted to OxyContin information.
2. Training Bulletins dealing with items brought up during the National Meeting Workshop discussions.
3. An interactive computer program featuring the "best" responses to handling objections (see illustration).
4. An interactive computer learning program featuring pain management case studies.
5. A videotaped panel discussion featuring Purdue Pain Management Specialists.
6. District Meeting Workshops dealing with OxyContin selling Issues.

Even more OxyContin support programs are in the works. Good luck in earning big bonus $$$ with OxyContin Tablets!! We will continue to give you all the help you need. ■




# Welcome to the Home Office...

Lauren Botticelli

Lauren has recently been promoted to the position of Marketing Associate, Sales Training.

Lauren began her career with Purdue in September of 1986 as a Senior Clerk in our Accounting Department. From there, she moved through Marketing and Sales Administration, rising to the position of Assistant Manager, DDD. In 1991 Lauren was promoted to Sales Representative, in the New England South District. Her accomplishments within her district include Topper's Winner in 1993, and a promotion to Professional Representative in 1994.

Lauren has relocated to Shelton, Connecticut.

Jim Gill

Jim joined the Purdue Frederick Home Office on November 1, 1995, as Marketing Associate. In his new position, Jim reports to Mike Cullen, Group Product Manager.

Jim started his career with Purdue in 1993 as a Professional Sales Representative in the Independence District. Prior to this, he was a Professional Medical Representative at Syntex Laboratories, Inc.

Jim and his wife, Donna, now live in Fairfield County. ■


**Teamlink**

Volume 11, Number 1

*Editor:* Lisa La Blanc
*Published by:* Training & Development

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100 Connecticut Avenue
Norwalk, CT 06850-3590

# Taking Home the "Wampum"!

## Wigwam Contest Winners

### Managed Health Care Account Executives

Mike Heinzman, Eastern Area (Tie)
Lynn Nagorski: Western Area
Joe Saiz: Eastern Area (Tie)

### National Accounts Manager

April King, Columbus Ohio

### Eastern Region District Winners

*Left to Right:*

| | |
|---|---|
| Andy Ritter | New England North |
| John Walters | Liberty |
| Susan Topalian | Hudson Valley |
| Carol Robertson | New England South |
| Gary Hinds | Knickerbocker |
| Tony Morello | Independence |
| Bobbi Sobel | Chesapeake |
| Pat O'Conner | Keystone |
| Craig Waringa | Empire |


### Southern Region District Winners

*Left to Right:*

| | |
|---|---|
| Jim Lucas | Hurricane |
| Frank Glen | Dixie |
| Richard Tankersly | Gulf |
| Kelly Crew | South Atlantic |
| Ronnie Russell | Delta |
| Carol Detzel | Sunshine |
| George Baihly | Capital |
| David Gulledge | Vulcan |
| Hector Berlingeri | Puerto Rico |
| Dave Stewart | Mardi Gras |

## Central Region District Winners

*Left to Right:*

| | |
|---|---|
| Tamara Mullin | Great Lake North |
| Suzanne Albers | Pacer |
| Stephen Musich | Buckeye |
| Rich Querierra | Allegheny (tie) |
| Karen Kralik | Allegheny (tie) |
| Dennis Chandler | Speedway |
| Jerry Mendel | Allegheny (tie) |
| Mary Beck Johnson | Viking |
| Given Graves | Great Lake South |
| Pat Crilley | Pioneer |
| Cara Monnig | Plains |


## Western Region District Winners

*Left to Right:*

| | |
|---|---|
| Pat McGowan | Olympic |
| Alan Sloan | Grand Canyon |
| Dennis Sagendorf | Mile High |
| Kerry Miller | Cimarron |
| Jeff Dulcie | Armadillo |
| Holly Hendrix | Mission |
| Michele Ringler | L.A. North |
| Steve Johnson | Golden Gate |

## Eastern Region

Keystone District - John Arent, DM

## Southern Region

Mardi Gras District - Dennis McCann, DM

## Central Region

Allegheny District - Bill Gergely, DM

## Western Region

Cimarron District - Gene Snook, DM

# Long Term Relationships

**Lou LaJoe**
*30 years*
*Buckeye District*

**Syd Jacobson**
*25 years*
*Great Lake North District*

*SPEECH continued from page 2*

OxyContin was brought to NDA filing from early Phase I work on time and in an incredibly compressed period of two years time. Robert Reder set the goal in November of 1993 to file by December 31, 1995, and we submitted on December 28, 1995, three days ahead of schedule. This didn't "just happen." It was a deftly coordinated, planned event that took dozens of worker-years of effort to succeed.

The most demanding NDA package for any analgesic product ever submitted didn't languish at the Agency. Unlike the years that other filings linger at FDA, this product was approved in 11 months, 14 days. Our previous best approval time for other products was measured in years, not months!

Much of this can be attributed to the unparalleled teamwork of the product team and FDA's approval team which came into being as a response to our joint desires to operate within the context of a new time frame. Both we and the Pilot Drug division at the FDA were motivated by the same goal, to get the highest standard NDA with the broadest indications approved in the shortest possible time frame.

Another first was that right from the beginning we designed the program to be international. Robert Kaiko accepted the challenge to achieve an approval in Europe simultaneously with our planned approval in the US, an almost impossible feat. Well, it was not quite accomplished. But I have the distinct honor and privilege to tell you that only 28 days after the US approval, we today received our first European approval for OxyContin Tablets! The best previous time between European and US approvals was measured in years, not in days! I love this business!

Paul wanted me to tell you that the approval would have been virtually simultaneous but for an unprecedented snow storm in Scandinavia on the day the committee was to meet to agree on approval. So this blizzard is not the first time that snow has play a powerful and prophetic role in the fortunes of OxyContin Tablets.

But OxyContin Tablets spawned another benefit, which you will all come to appreciate in the months and years to come. As the NDA was being filed, we all realized that this fast research program was an approach that we wanted to repeat, but we were not satisfied with the pace of development of other active projects during the two years that OxyContin was speeding toward filing.

Things are changing faster, and we must develop products faster than previously in order to grow as we want to grow. Developing products faster means getting our product portfolio approved faster, not one product every few years.

So at Paul Goldenheim's urging, we placed product development, medical research and NDA filings on the alter of the Church of Reengineering.

In some companies, the Church of Reengineering is associated with a formerly archaic practice of Human Sacrifice.

But like many things that we do, we had a different notion of means and ends. Our goal was to find out how to bring to effective approval a number of projects like OxyContin **simultaneously.** And we reasoned that increased efficiency would allow for this end without Human Sacrifice. We would research the entire portfolio at OxyContin speed!

So at great cost and effort, a mixed management team went to work to reengineer our product development and medical research efforts. The result is not a smaller R&D and Medical Department, but a dynamically growing one, with no less than five projects advancing simultaneously toward planned NDA filings from 1997 through 1999 just as OxyContin rocketed to filing in the 1994-1995 period.

These differences then are some of the measures of the expanding commitment of the Sackler family to our business, here and world wide.

Other measures include: doubling research investment in the past three years; building sales and marketing forces here and abroad, adding corporate development staff, and branching out into other markets including China, India, and South America and Japan.

In Japan, almost as large a pharmaceutical market as the US, we are gearing up for major new initiatives, both in terms of partnerships with our products, and in-licensing of other major company's products.

Just a week ago, we made our first offer for a product invented in Japan. We sent to the President of one of the top five companies a multi-million dollar offer for exclusive, worldwide rights (excluding Japan, of course) for a new compound in a new class for the treatment of asthma and potentially other serious medical conditions. Although this was our first effort in this regard, it will not be our last.

We are investing globally which doesn't mean only abroad, but even more so here, at home. These global developments are at the expense of the US operations, but fundamentally in support of our growth here as well.

The US is the site of almost 50% of our sales. The US was and is our fastest growing company anywhere. We grew faster than any operation in the group in 1995! Congratulations! And thank you; thank you very much. And in 1996, I fully expect that it will have the highest rate of growth again, both in absolute amount and in percentage.

We fully expect OxyContin Tablets to surpass the sales of MS Contin Tablets very quickly, not because MS Contin Tablets is declining, but because OxyContin Tablets will so much more effectively address a much, much bigger market! And I expect that this will happen before the end of the decade.

How am I so sure? Because I know what kind of team we have working with you behind the scenes, and I know that you are the Greatest Sales Force on Earth.

Thank you, and good evening. ■

# Leading the Way...

... in Managed Healthcare

Eastern Area
*Left to right:* Mel Grayson, Joe Saiz, Dave Wallen, Mike Heinzman, Bob Vlk, Nick Primpas, Gary Norbury, *Manager,* and Rhys Thomas

## ... in National Accounts

| | |
|---|---|
| April King | Columbus, Ohio |
| Shelton Benson | Texas |
| G.R. Green | (Executive Director) |
| Charlene Agurs | New Jersey |
| Dan Pearson | Los Angeles |
| Tony Scifo | Chicago |
| *missing from photo:* | |
| Steve Bishop | Washington, D.C. |

Western Area
*Left to right:* Brett Ciricillo, Sharon Gibbons, Randall Johnston, Lynn Nagorski, Tim Richards, *Manager,* and Sabrina Taylor

## The Inspiration of Diana Golden

**Left:** Diana and her "permanent on-stage sidekick," Midnight!

**Right:** Diana and her "temporary on-stage sidekick," Max!

**Max Gessner, Sunshine District**

# Pain Management Meeting

*Jerry Pizzola*

To maintain the sales momentum of OxyContin™ Tablets, Purdue's Medical Education department invited health professionals from all over the country to attend an educational seminar in San Antonio, Texas. The purpose of this meeting was to educate these potential speakers about OxyContin so they can speak about it intelligently and answer questions appropriately.

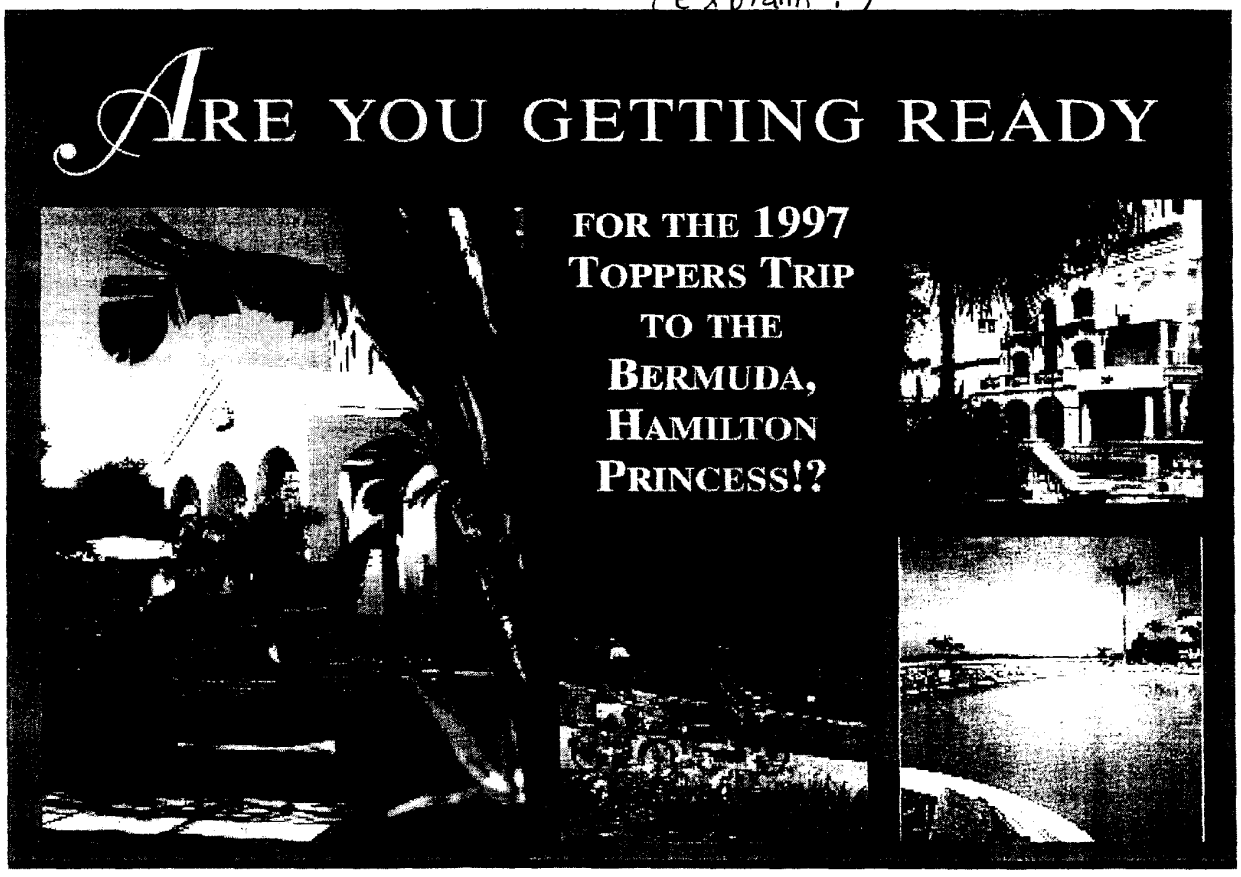
Terry Newell, Sharon Green, and Christine DiDomenico met the arriving parties at the reception desk. Almost immediately, every one was separated into one of four rooms where they were educated on the product and asked for feedback of what they perceived as potential issues that they may hear about during or after a presentation. Attending this meeting was an assortment of specialists, including oncologists, nurses, orthopedic surgeons, primary care physicians, and hospital-based pharmacists.

PHOTO

On Saturday, attendees were presented the results of the OxyContin clinical trials and a testimonial from one of the clinical investigators. Drs. Robert Reder and Robert Kaiko thoroughly explained the results of the clinical trials needed to file the INDA. After each session, participants clarified any questions by addressing them to Dr. Reder and Dr. Kaiko and to the entire audience. Dr. Elizabeth Narcessian, an physiatrist from the Kessler Institute in East Orange, New Jersey, spoke about the positive responses seen from her patients taking OxyContin. The hush from the audience showed that they, too, wanted to experience these results with their patients. In addition, these participants will have the opportunity to affect more patients by speaking to their colleagues about pain management.

Sunday brought a delightful, energetic Joyce Newman to the stage. Ms. Newman enthusiastically explained how participants, as speakers, could make "Powerful Presentations."

The program was a resounding success! Medical personnel left the meeting with answers to issues such as *pharmacy availability, cost vs. Percocet® and MS Contin®, Managed Health Care formulary-availability, and differences in speaking to "cancer" physicians vs. "non-cancer" physicians.* Most importantly, they left with a better understanding of the features and benefits of OxyContin. ■



# Recent Promotions

## Managed Health Care

**Brett Ciricillo**
*Managed Health Care AE*

As of November 1, 1995 Brett assumed the position of Western Area Account Executive, Managed Health Care. Brett's accomplishments since joining Purdue in February of 1991 include: District Representative of the Year, Toppers Winner, Promotion to Medical Marketing Representative, MS Contin® Specialist, and District Field Trainer.

Brett, his wife, Melissa, and their one-year old son live in Cincinnati, OH.

## District Managers

**Jeff Strada**
*Gulf District*

In November of 1995, Jeff was promoted from Professional Representative in the Hurricane District to the position of District Manager of the Gulf District, reporting to Windell Fisher.

Jeff joined Purdue in June of 1993, and quickly earned Toppers Club Membership in 1994. By the second quarter of 1995, Jeff ranked #36 in the Toppers Club contest. Jeff's professional experience prior to Purdue includes being a Medical Representative for Basel Pharmaceuticals/ CIBA-GEIGY Corporation, and an Account Executive for Abbey Home Healthcare.

Jeff and his wife, Pam, and their children now reside in Kingwood, TX.

**Gene Snook**
*Cimarron District*

Gene has recently been promoted from being a Medical Marketing Representative in the Olympic District to the position of District Manager of the Cimarron District. Gene joined Purdue in October, 1990. Some of his successes since then include: Toppers Club membership in 1991, 1993, and 1994; Presidents Council, 1993, and 1994; District Field Trainer, MS Contin Product Specialist; Western Region Alferon N® Task Force member; and promotion to Medical Marketing Representative in October of 1993. Prior to joining Purdue, Gene was a District Sales Manager for Whitehall Laboratories in Portland, Oregon.

Gene, his wife, Carol, and their children have relocated to Edmond, Oklahoma.

**Joe Hennessey**
*Speedway District*

Joe Hennessey, formerly Account Executive, Managed Health Care in the Western Area, has been promoted to the position of District Manager of the Speedway District.

Since the start of Joe's career at Purdue in January of 1991, Joe has held the following responsibilities: 1992 and 1993, Central Region District Field Trainer; April 1993, Medical Marketing Representative; August 1994, Account Executive, Managed Health Care.

Prior to joining Purdue, Joe worked as a Pharmaceutical Representative for Adria Laboratories in Indiana.

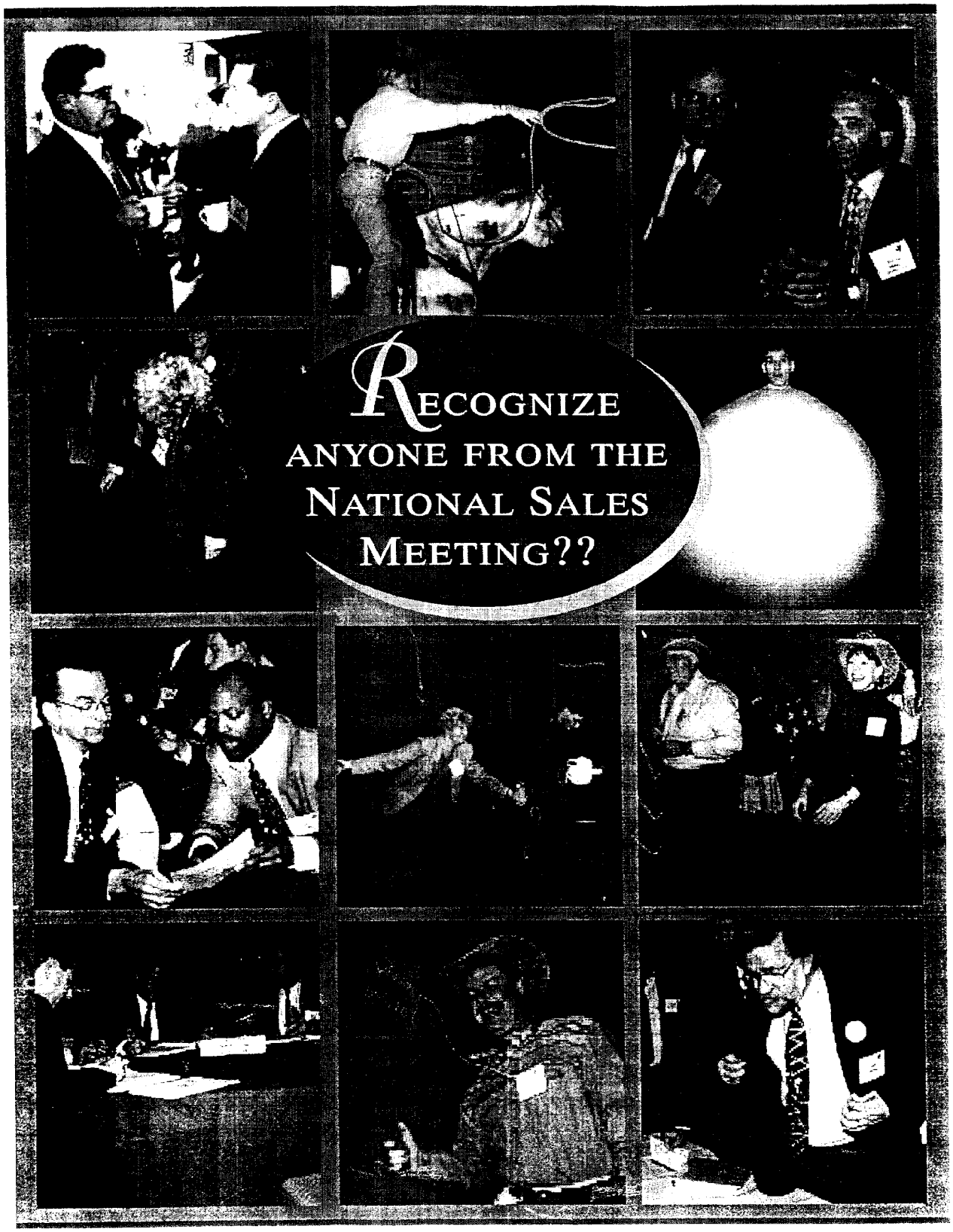
Joe lives in Indianapolis, Indiana.

**Kelly Bartlett**
*Independence District*

In October of 1995, Kelly assumed responsibility as District Manager for the Independence District. Since the start of his career with Purdue, Kelly has served the Eastern Region as District Field Trainer, led the Viking District as District Manager, and served as a Medical Marketing Representative in the New England/North District.

Kelly joined Purdue in 1990. Prior to that, he was employed as a Medical Representative with Stuart Pharmaceuticals.

Kelly, his wife, Heidi, and their children have relocated to Jamison, PA.

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CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER

PKY180280962

# Exhibit 4

## Unknown

**From:** Dr Kathe Sackler
**Sent:** Tuesday, August 05, 1997 4:04 PM
**To:** Dr Kathe Sackler
**Subject:** Re[3]: OXYCONTIN

Dear Dr. Richard,

Please be informed that Harry Kletzko will prepare the requested 5 year forecast until the end of this week.

Best regards,

Irene Lahnstein
- Assistant to Mr. Wimmer -

_____ Reply Separator _____

Subject: Re[2]: OXYCONTIN
Author: Dr Richard Sackler at NORWALK
Date: 02.03.1997 13:12

THIS IS THE FIRST TIME I HAVE HEARD OF THIS IDEA.

WHAT MAKES US BELIEVE THAT WE CAN ACCOMPLISH IT? WALTER, HOW SUBSTANTIALLY WOULD IT IMPROVE YOUR SALES? PLEASE GIVE A FIVE YEAR PROJECTION WITH CONTROL AND WITHOUT.

DOES EACH MEMBER OF HE EU DECIDE THIS FOR THEMSELVES, OR WOULD ONE LEAD? IF ONE WOULD LEAD, THEN IS DENMARK OR GERMANY MORE LIKELY TO AGREE?

_____ Reply Separator _____

Subject: Re: OXYCONTIN
Author: Dr Robert Kaiko at NORWALK
Date: 2/27/97 12:43 PM

While my thinking is still developing, frankly, I am very concerned, and I would have to recommend against the "uncontrolled/but monitored" proposal at this time (perhaps, if only to make sure the risks are appreciated and accepted before we proceed as proposed):

a) while I am told that BfArM is not unwilling to hear our case for an uncontrolled status for OxyContin, BfArM may view our proposal as irresponsible; this could be damaging to our overall relationship with them and to their view of OxyContin;
b) I don't believe we have a sufficiently strong case to argue that OxyContin has minimal/or no abuse liability:
   - in the U.S. oxycodone containing products were once less controlled than now; abuse resulted in greater controls;
   - oxycodone containing products are still among the most abused opioids in the U.S.; this information is available to BfArM;
   - the local tissue necrosis that can result from injection of OxyContin "fixed" for such abuse is not likely to be a deterrant to abuse; let us not forget that in New Zealand, MST is the most common sources of parenterally abused

morphine/heroin;
- our dossier acknowledges a small handful of patients in our research program who were suspect in terms of their drug accountability;
- we do not have a postmarketing abuse monitoring system and data base from which we could conclude that diversion/abuse is not occurring.

c) If OxyContin is uncontrolled in Germany, it is highly likely that it will eventually be abused there and then controlled. This may be more damaging to OxyContin internationally than any temporarily higher sales that would be gleaned from an uncontrolled status; let us not forget the experience with buprenorphine, which was initially uncontrolled: reports of abuse in Germany, in part, eventually led to lots of bad press and controlled status; worldwide sales suffered - even where buprenorphine had been already controlled.

So, given the above, what do others have to offer that should prompt us to pursue the proposal for uncontrolled status for OxyContin anywhere?

_____ Reply Separator _____

Subject: OXYCONTIN
Author: Walter Wimmer at MUNDIPHARMA-GERMANY
Date: 2/27/97 4:53 PM

Dear Bob,

I am referring to the telecon that you had with our Registration Officer, Matthias Görich, to prepare the meeting with the BfArM on March 7, 1997.

In the course of this conversation he explained to you that due to his discussions with the BfArM he does see a 50% chance to get Oxycontin off the Narcotic Drug Status provided you could give some information on the very low abuse potential of our CR formulation.

The non-narcotic status of Oxycontin would mean a vast increase of the market potential in Germany because we could then like P.F. in the USA broaden the use of Oxycontin to non-malignant, especially arthritic pain.

The non-narcotic drug status of Oxycontin would not merely mean "prescription only" but a "closely monitored prescription only status" for a certain period of time during which, e.g. we have to keep the BfArM fully informed on any incidents of abuse. In practice this meant that our salesreps would have to ask the physicians routinely whether they have become aware of abuse of Oxycontin in any of their patients put on the product.

If Oxycontin remained a narcotic it would be used for cancer pain only and thus sooner or later substitute MST.

I have discussed this concept with Dr. Mortimer and he said we should try this by all means. I have also discussed the necessity to conduct a clinical trial with Oxycontin in Germany for marketing reasons. He is also in favour of such study and advised that Dr. Fleischer should liaise with you and Dr. Goldenheim.

Best regards,

W. Wimmer

# Exhibit 5

**Unknown**

**From:** Dr Richard Sackler
**Sent:** Wednesday, April 23, 1997 10:53 AM
**To:** Michael Friedman
**Subject:** Re[3]: San Antonio

**Importance:** Low

excellent points.

what about rifle shots?

_____ Reply Separator _____

Subject: Re[2]: San Antonio
Author: Michael Friedman at NORWALK
Date: 4/22/97 3:19 PM

Richard,

There will always be misconceptions about drug substances. For controlled release drugs, many of these misconceptions are the result of residual attitudes associated with the immediate release forms. For example, morphine has a "personality" that was shaped when it was an IV drug. Oxycodone has a "personality" that is influenced by many years of oxycodone use in Percocet. We have built a large part of our platform on this personality and used it to differentiate OxyContin from MS Contin and Duragesic. This differentiation has lead to much non-malignant business.

Marketing is not only about what you are. It is also about what you are not. We have a success beyond our expectations that is,in part, due to the unique personality of OxyContin. Even as we seek to increase the use of the drug in higher doses, we should be very careful. As far as I know, the strength of the drug is principally a barrier in malignant pain. We do not want to change the image in a way that will discourage non-malignant use. A barrage would be ill advised.

MF

_____ Reply Separator _____

Subject: Re: San Antonio
Author: Dr Richard Sackler at NORWALK
Date: 4/22/97 11:45 AM

Michael,

I am somewhat surprised that 18 months into marketing, significant groups of experts (oncologists, for example) believe that oxycontin has a ceiling effect.

What materials could we pull together that would smash this critical misconception? Can we put together some approaches and test whether they would be potent weapons in this effort?

_____ Reply Separator _____

Subject: San Antonio
Author: Michael Friedman at Norwalk
Date: 4/21/97 5:10 PM

fyi

Forward Header

Subject: San Antonio
Author: James J Lang at NORWALK
Date: 4/20/97 10:04 AM

Mark

I sat in on one of the Oncology Focus groups on Friday evening. You will have an opportunity to listen to the tapes and whatever summaries the focus group moderators provide, however it appears the issues effecting Oncologist's utilization of OxyContin are and continue to be

- MD's feel the product dosing has a ceiling
- Don't feel it is as strong as Ms Contin
- Like and are very comfortable with Ms Contin and don't see a need for another product except where Ms Contin fails.

Interestingly, when asked to describe what they like about OxyContin they for the most part cited all the key points our reps are or should be stating in their sales presentations. This observation was similar to the others who attended the other Oncology focus group.

The anesthesiology focus group Saturday evening was of less value however their primary concerns were the Medtronic pump being used by the orthopods and the need for Purdue to educate surgeons on proper post surgery pain management, and fears with opiod prescribing.

As we prepare for the up coming one day district meetings the above topics should part of the focus for our training. Any suggestions your people may have would be appreciated.

jim

Subject: San Antonio
Author: Michael Friedman at Norwalk
Date: 4/21/97 5:10 PM

fyi

Forward Header

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Author: James J Lang at NORWALK
Date: 4/20/97 10:04 AM

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- Don't feel it is as strong as Ms Contin
- Like and are very comfortable with Ms Contin and don't see a need for another product except where Ms Contin fails.

Interestingly, when asked to describe what they like about OxyContin they for the most part cited all the key points our reps are or should be stating in their sales presentations. This observation was similar to the others who attended the other Oncology focus group.

The anesthesiology focus group Saturday evening was of less value however their primary concerns were the Medtronic pump being used by the orthopods and the need for Purdue to educate surgeons on proper post surgery pain management, and fears with opiod prescribing.

As we prepare for the up coming one day district meetings the above topics should part of the focus for our training. Any suggestions your people may have would be appreciated.

jim

**Unknown**

**From:** Dr Richard Sackler
**Sent:** Tuesday, April 22, 1997 11:46 AM
**To:** Michael Friedman; Dr Paul Goldenheim
**Cc:** James J Lang
**Subject:** Re: San Antonio

**Importance:** Low

Michael,

I am somewhat surprised that 18 months into marketing, significant groups of experts (oncologists, for example) believe that oxycontin has a ceiling effect.

What materials could we pull together that would smash this critical misconception? Can we put together some approaches and test whether they would be potent weapons in this effort?

Reply Separator

Subject: San Antonio
Author: Michael Friedman at Norwalk
Date: 4/21/97 5:10 PM

fyi

Forward Header

Subject: San Antonio
Author: James J Lang at NORWALK
Date: 4/20/97 10:04 AM

Mark

I sat in on one of the Oncology Focus groups on Friday evening. You will have an opportunity to listen to the tapes and whatever summaries the focus group moderators provide, however it appears the issues effecting Oncologist's utilization of OxyContin are and continue to be

- MD's feel the product dosing has a ceiling
- Don't feel it is as strong as Ms Contin
- Like and are very comfortable with Ms Contin and don't see a need for another product except where Ms Contin fails.

Interestingly, when asked to describe what they like about OxyContin they for the most part cited all the key points our reps are or should be stating in their sales presentations. This observation was similar to the others who attended the other Oncology focus group.

The anesthesiology focus group Saturday evening was of less value however their primary concerns were the Medtronic pump being used by the orthopods and the need for Purdue to educate surgeons on proper

post surgery pain management, and fears with opiod prescribing.

As we prepare for the up coming one day district meetings the above topics should part of the focus for our training. Any suggestions your people may have would be appreciated.

jim

# Exhibit 6

Author: Dr Richard Sackler at NORWALK
Date: 5/28/97 8:00 PM
Priority: Normal
TO: Michael Friedman at NORWALK
Subject: Re[2]: oxypblms.doc

re OxyContin

---------- Message Contents ----------

I agree with you. Is there general agreement, or are there some holdouts?

---------- Reply Separator ----------

Subject: Re: oxypblms.doc
Author: Michael Friedman at NORWALK
Date: 5/28/97 1:15 PM

My purpose in writing this memorandum is to clarify our position on the very complex issues raised by Mike Cullen during the Phase IV team meeting and which were the subject of Dr. Richard's inquiry.

We are well aware of the view, held by many physicians, that oxycodone is weaker than morphine. We all know that this is the result of their association of oxycodone with less serious pain syndromes. This association arises from their extensive experience with and use of oxycodone combinations to treat pain arising from a diverse set of causes, some serious, but most "less serious." This "personality" of oxycodone is an integral part of the "personality" of OxyContin.

When we launched OxyContin, we intentionally avoided a promotional theme that would link OxyContin to cancer pain. We specifically linked OxyContin to the oxycodone combinations with our "old way, new way" campaign. We made sure that our initial detail piece provided reps with the opportunity to sell the product for a number of different pain states. With all of this, we were still concerned that the drug would be slotted for cancer pain and that we would encounter resistance in the "non-malignant pain market."

Our pricing of the product was geared toward the non-malignant market. We knew that if we priced low (per mg.)for the high dose cancer patient, we would be priced way too low (per mg.) for the "standard" non-malignant pain patient, where we really wanted to make a market. We feared that the "cancer pain experts" would object to the 2:1 ratio and resulting cost of therapy for high dose patients, however, we had no choice, given our chosen position for OxyContin. In any case, we are developing hydromorphone OD for the high dose patient.

Despite our initial uncertainty, we have been successful beyond our expectations in the non-malignant pain market. Doctors use the drug in non-malignant pain because it is effective and the "personality" of OxyContin is less threatening to them, and their patients, than that of the morphine alternatives. (I apologize for this unscientific term, but, I feel it captures the notion that there are image related attributes that influence drug acceptance.) While we might wish to see more of this product sold for cancer pain, it would be extremely dangerous, at this early stage in the life of this product, to tamper with this "personality," to make physicians think the drug is stronger or equal to morphine. We are better off expanding use of OxyContin, in the non-malignant pain states and waiting for Hydromorphone OD, in 1999, to relaunch into cancer pain.

**CONFIDENTIAL INFORMATION**

INF

For the time being, I do not plan to try to change the "personality" of OxyContin. We will continue to FOCUS on expanding the non-malignant pain usage. In this group of patients, morphine is not an alternative, and the price is correct.

We will continue to encourage doctors treating cancer patients to start earlier with OxyContin and avoid combinations. Hopefully they will achieve good results and keep these patients on OxyContin. For high dose patients we will study the possibility of limiting or holding the price increase on the 80 mg. However, I think that our real future in high dose cancer pain will be linked to hydromorphone OD.

I do not plan to spend too much time dealing with the 1:2 ratio issue. This is a red herring that is not relevant in the non-malignant pain market. We will provide our reps with the data and let them use it as needed to defuse situations where it will work for them.

MF

_____ Reply Separator _____

Subject: oxypblms.doc
Author: Dr Richard Sackler at NORWALK
Date: 5/25/97 2:54 AM

Please consider these continuing problems more than 20 months into the launch and promotion of oxy.

# Exhibit 7

From: Dr Richard Sackler
Sent: Thursday, June 12, 1997 5:40 PM
To: Michael Friedman
Subject: Re: OxyContin Team Meeting - Minutes

I think that you have this issue wellin hand. If there are developments, please let me know.

_____ Forward Header _____

Subject: Re: OxyContin Team Meeting - Minutes
Author: Michael Cullen at NORWALK
Date: 6/2/97 10:29 PM

In recent team meetings, we have discussed the issue that OxyContin is perceived by some physicians, particularly Oncologists, as not being as strong as MS Contin. Although this perception has had some effect with physicians switching to MS Contin with more severe cancer pain patients, it has actually had a positive effect with physicians' use in non-cancer pain.

Since oxycodone is perceived as being a "weaker" opioid than morphine, it has resulted in OxyContin being used much earlier for non-cancer pain. Physicians are positioning this product where Percocet, hydrocodone, and Tylenol with Codeine have been traditionally used.

Since the non-cancer pain market is much greater than the cancer pain market, it is important that we allow this product to be positioned where it currently is in the physician's mind. If we stress the "Power of OxyContin" versus morphine, it may help us in the smaller cancer pain market, but hurt us in the larger potential non-cancer pain market. Some physicians may start positioning this product where morphine is used, and wait until pain is severe before using it.

Marketing has decided that the efforts of the Phase IV Team should be predominantly focused on expanding OxyContin use for non-cancer pain. Our approach to cancer pain will be to get physicians to use it earlier, instead of products such as Percocet, Vicodin, and Tylenol #3. The sales force can teach the Oncologists to properly dose and titrate OxyContin to ensure that they "stay with" it as the pain increases. By doing this, the Oncologists will realize through experience that OxyContin is effective.

It is important that we be careful not to change the perception of physicians toward oxycodone when developing promotional pieces, symposia, review articles, studies, etc.

We can discuss this issue further at our next team meeting.

_____ Reply Separator _____

Subject: OxyContin Team Meeting - Minutes
Author: Linda Harrison at Norwalk2
Date: 6/2/97 4:43 PM

Attached are the OxyContin Team Meeting Minutes for 5/23/97.

# Exhibit 8

## Chasin, Mark

**From:** Chasin, Mark
**Sent:** Thursday, October 01, 1998 11:33 AM
**To:** Van Buskirk, Glenn; Palermo, Philip; Tonelli, Fred; Oshlack, Ben; Tigner, Joseph
**Subject:** FW: Performance Enhancing Agents

FYI

-----Original Message-----
**From:** Sackler, Dr Richard
**Sent:** Monday, September 28, 1998 10:21 PM
**To:** Alfonso, Mark; pdg; rmb; Chasin, Mark; Oshlack, Ben; bk; mf; Kyle, Don
**Cc:** KAW; Garbett, Dr Neil; rrs; Fleischer, Dr Wolfgang; MDS
**Subject:** FW: Performance Enhancing Agents

Kathy Walsh has surveyed a number of papers on Performance Enhancing Agents. The literature has called these "Lifestyle Drugs" but I prefer our designation. Regardless of the name used, a considerable number of agents that might be viewed as therapeutic clearly have a substantial profile as PEA's. Among them are agents such as Viagra, MS Contin Tablets and OxyContin Tablets.

I would urge each of you to read these two attachments. The viewpoint that I would suggest you consider is to take this perspective as one that may be enlightening, but more important, may inspire new ideas. Our historic view of our mission is to devise agents that provide treatments for or amelioration of diseases or their signs and symptoms. The PEA departure is to broaden our perspective to include agents that enhance personal performance. The attached article says that this is particularly relevant as the B Boombers enter advaced age, but I would suggest that the relevance (if indeed it has anything to recommend it) is that it will liberate us to seek and develop enhancements that may be related to diseases or their effects or may stand on their own merits. Memory enhancement drugs may be particularly needed as memory fails with advancing years and organic brain diseases, but it might well be that a memory enhancing agent that worked at all ages would have substantial relevance to people who display normal age appropriate memory even in their younger years.

If this effort is of any value, it will encourage us all to broaden our perspectives of opportunities for invention.


LIFESTY1.DOC


LIFESTBW.DOC

*Richard Sackler, M.D.*
**Telephone** 203 854 7100
**Internet address** rss@pharma.com
**Voice mail** 203 855 8800 / 47100#

-----Original Message-----
**From: Walsh, Kathy**
**Sent:** Monday, September 28, 1998 11:41 AM
**To:**Sackler, Dr Richard
**Subject:** Performance Enhancing Agents

Richard,

As we have discussed, I put together some notes from recent articles on a category of drugs referred to as "lifestyle drugs". This is a term the media has coined, which is not accepted by the major pharmaceutical companies, but which comes close to identifying the kinds of performance enhancing agents you requested information on. The term "performance enhancement" itself is almost exclusively used in publications to refer to substances banned by athletic organizations.

The attached file LIFESTY1.DOC contains my notes. The file LIFESTBW.DOC has an article from Business Week which was a good summary of the topic. It also includes an additional article on enhancing performance that I thought might be of interest.

# Exhibit 9

Naturally this works for me. Richard Sackler, M.D. 7100 in Norwalk Internet rss@pharma.com Intranet http://library.pharma.com/directory/TelephoneNumber.asp?as_tel=7100&B1=Search Local time in Connecticut 10/13/99 12:29:25 PM -----Original Message----- From: Haddox, Dr. J. David Sent: Wednesday, October 13, 1999 12:20 PM To: Sackler, Dr Richard; Sackler, Dr Raymond R; Reder, Robert; Kaiko, Dr Robert; Wright, Dr. Curtis; Goldenheim, Paul; Lacouture, Dr Peter; Haskell, Dr. Lloyd Cc: Howard, Linda Subject: FW: RE: Re: Re: Lecture in Boston Dear Colleagues, I am forwarding this information to request that you check your availability for these dates. The MSPREP at Tufts wants to have a "launch" symposium on pain, and they have invited Dr. David Niv, who is a well known pain physician on the faculty of the Sackler School of Medicine in Tel Aviv. This is a seminal event for the Master's Program, the first of its kind in this hemisphere, and they obviously would like to have a good representation from the company in attendance. Please let Ms. Linda Howard know how this fits your schedules. Thank you. jdh PS: If I have left anyone out unintentionally, please advise. -----Original----- From: Daniel Carr [SMTP:daniel.carr@es.nemc.org] Sent: Wednesday, October 13, 1999 10:02 AM To: Dr.J.David.Haddox@pharma.com Cc: KCB12444@aol.com; KLasch@Lifespan.org; Evelyn Hall Subject: re: RE: Re: Re: Lecture in Boston Dave, FYI I just spoke with Richard Sackler and he indicated that late Monday Dec 6 or 4-5 PM Weds the 8th of December would work best for him -- particularly the latter as he has to be in Boston anyway to teach a class in the MD/MBA program. By copying this e-mail to Ken Blaisdell and Kathy Lasch, I'll ask that they vote on which if any date would be best for them. If you could check things out at Purdue, then everyone got back to me in the next couple of days, we could make plans for this kick-off event. Look forward to hearing from you, Dan

# Exhibit 10

Dear Colleagues,

Some of you have expressed concern about an article in this week's *Time* magazine, "The Potent Perils of a Miracle Drug," which unfortunately emphasizes the abuse and diversion rather than the therapeutic qualities of our leading product, OxyContin®.

We were aware that this article was in the works, and we tried to make the reporter understand our messages about the need for treating people in pain. Unfortunately, we didn't succeed, and the article presents anything but a balanced account.

However, the same issue of *Time* included a positive story about the new JCAHO pain standards in its "Your Health" column – bringing a certain amount of fair balance to that publication.

Dr. David Haddox, Purdue's Senior Medical Director, Health Policy, has written a Letter to the Editor of *Time* in which he expresses the points we hoped would have been included in a more balanced article. We expect a similar letter to be written by the American Pain Foundation, on behalf of the "pain community."

I believe that the negative impact of the *Time* article will be more than offset by a significant number of balanced, accurate articles that have appeared in other publications and on television programs in the past week or so. As you may know, the new JCAHO (Joint Commission on Accreditation of Healthcare Organizations) pain standards went into effect on January 1, which explains the unusual amount of attention that this subject is receiving.

The Library has compiled highlights of this excellent media coverage for our Intranet site. Several positive articles, along with Dr. Haddox's Letter to the Editor, can be accessed at the links shown below.

As OxyContin® tablets continues to expand its market share, we are bound to become an even larger target for sensational reports in the media. Nevertheless, we intend to stay the course and speak out for people in pain – who far outnumber the drug addicts abusing our product. We cannot allow ourselves to be discouraged by negative press as we continue to focus upon our noble mission.

Richard S. Sackler, M.D.

# Exhibit 11

From: Sackler, Dr Richard
Sent: Thursday, February 01, 2001 11:57 PM
To: [redacted] (E-mail)
Subject: FW: Unique Valentine gift ideas from [redacted]

Dear [redacted],
Thank you so much for your analysis and support. I agree 100%. But we will have to mobilize the millions that have serious pain and need our product. This we will try to do.
Meanwhile, we have to hammer on the abusers in every way possible. They are the culprits and the problem. They are reckless criminals.

Richard S. Sackler, M.D.
President, Purdue Pharma, L.P.
Laptop 2000 machine
One Stamford Forum
Stamford, CT 06901
Telephone [redacted] new number
Internet [redacted]
Intranet http://library.pharma.com/directory/
Located in Connecticut

---Original Message---
From: [redacted]
Sent: Friday, February 02, 2001 3:27 PM
To: Sackler, Dr Richard
Subject: RE: Unique Valentine gift ideas from [redacted]

I think that you have already stated the central truth.
Nobody is speaking for the patients in pain.

Supporting facts and principles:
1. analgesic efficacy correlates with potential for abuse (an alternative drug would have the same problem) If it is abused, that is because it is so GOOD for legitimate uses;
2. narcotic control measures must not interfere with the appropriate use of drugs;
3. any control scheme which allows appropriate use CAN be circumvented by abusers;
4. Purdue has done nothing to encourage abuse and in fact has taken measures to discourage inappropriate use;
5. decreasing narcotic availabilty increases patient suffering and other morbidity;
6. any alternate drug with comparable effectiveness will be abused to the same extent (see #1)
7. this is a problem caused by addicts and illegal drug dealers. Why isn't 60 minutes asking those jerks why they want to divert a necessary drug and make it less avialable to people who need it?
8. the problem is the aberrant behavior of certain individuals. They are the real problem and the real news story.

I hope that this is helpful.

I might not check this mailbox again. I created it to send the promo mail. Please continue to correspond with me

via [redacted], or [redacted](same box).
I plan to be in PNH until 8 Feb.

Good luck. Illegitemi Non Carborundum ! Don't let the
bastards grind you down.

[redacted]

-----Original Message-----
From: "Sackler, Dr Richard" <[redacted]>
Date: Thu, 1 Feb 2001 08:53:01 -0500
Subject: RE: Unique Valentine gift ideas from [redacted]

> Thanks for the advertisement from [redacted]. I'll study it later today.
> We got a rumor that 60 Minutes is nosing around. How do we deal with
> this?
> This is tough. I am totally outside my element. The damage done to
> patients by the Time article is unknown, but serious, I'm sure. This
> campaign has attracted a lot of attention. No one is speaking for
> the
> patients in pain.

# Exhibit 12

From: Sackler, Dr Richard
Sent: Thursday, February 08, 2001 9:59 PM
To: Hogen, Robin; Haddox, Dr. J. David; mxf; hru
Cc: pdg; eda; edm
Subject: FW: NYTimes.com Article: Cancer Painkillers Are Being Abused

This is not too bad. It could have been far worse.

Thanks for all the support.

Richard S. Sackler, M.D.
President, Purdue Pharma, L.P.
Laptop 2000 machine
One Stamford Forum
Stamford, CT 06901
Telephone 203 588 7777 new number
Internet rss@pharma.com
Intranet http://library.pharma.com/directory/
Located in Connecticut

-----Original Message-----
From: msackler@me.net [mailto:msackler@me.net]
Sent: Thursday, February 08, 2001 10:33 PM
To: rss@pharma.com
Subject: NYTimes.com Article: Cancer Painkillers Are Being Abused

This article from NYTimes.com
has been sent to you by msackler@me.net.

Here it is


Cancer Painkillers Are Being Abused
February 9, 2001

By FRANCIS X. CLINES with BARRY MEIER
LEXINGTON, Ky., Feb. 8 - Harried police detectives in dozens of rural areas in Eastern states are combating what they say is a growing wave of drug abuse involving a potent painkiller prescribed for terminal cancer patients and other people with severe pain.
Illicit dealers have used suffering patients as well as fakers, the authorities report, to "doctor shop" to obtain the drug, OxyContin, for resale. Addicts favor the drug because they have learned to circumvent its slow time-released protection and achieve a sudden, powerful morphine-like high.

OxyContin is often covered under health care plans. Police say that when dealt illicitly on the street it can cost as much as heroin or more. The abuse of the drug, which has been tracked over the last 18 months, has set off a wave of pharmacy break-ins, emergency room visits and arrests of physicians and other health care workers.

Along with Kentucky, law enforcement officials have cited a troubling number of cases in Maine, Maryland, Ohio, Pennsylvania, Virginia and West Virginia.

"Heck, we already know it's pretty epidemic down here," said Capt. Minor Allen of the Hazard police in southeastern Kentucky, where federal, state and local police rounded up scores of purported dealers and users this week. The authorities say dozens of deaths may be laid to OxyContin abuse, but this is strongly disputed by the manufacturer, Purdue Pharma of Norwalk, Conn.

"Abuse of this drug has become unbelievable in the last year with probably 85 to 90 percent of our field work now related to oxys," Captain Allen said, using street shorthand for the drug.

The drug's active ingredient is oxycodone, a morphine-like substance that is also found in drugs like Percodan and Tylox. But while painkillers like Tylox contain five milligrams of oxycodone and require repeated doses to achieve pain relief, OxyContin contains 40 to 160 milligrams in a time-released formulation that controls pain over a longer period. Chewing or crushing the prescription pill foils its time-release protection, delivering an instant potent euphoria. Once crushed, the drug can be snorted by addicts or dissolved for injection. And this new addiction has occasioned a telltale bit of fresh paraphernalia among teenage abusers, Captain Allen said.

"We find them carrying pill crushers that are sold in drugstores to help elderly people swallow their prescriptions," he noted of a growing drug culture in which the Perry County park has come to called Pillville.

The abuse first drew alarm in Maine 18 months ago in rural, eastern areas not previously considered drug problems, Jay P. McCloskey, the United States attorney for Maine, said.

"What is most unusual and disturbing is the number of high school kids and those in the early 20's who got addicted," Mr. McCloskey said. "We are talking about some of the best students, some of the best athletes," he said, noting that his small state was among the nation's largest consumers of OxyContin on a per- capita basis.

The problem became so urgent in Kentucky that Joseph L. Famularo, the United States attorney for the eastern district of the state, directed the roundup of 207 suspects this week in Operation Oxyfest 2001, a nine- month investigation that produced the biggest drug-abuse raid in state history.

"I personally counted 59 deaths since January of last year that local police attributed to addicts using the drug, and I suspect that's pretty conservative," Mr. Famularo said, noting that cancer patients build a tolerance for the drug while a neophyte abuser may try it and be lethally stricken.

That number was disputed by the drug's maker. Dr. J. David Haddox, medical director for Purdue Pharma, said, "I'm concerned about inflammatory statements like that." He said that overdose deaths typically involve multiple factors like alcohol, and that exaggeration of abuses may cause physicians to deny the drug to suffering patients.

Why so many current abuses seem focused across stretches of Appalachia and other rural areas is an open question. But authorities note that the prevalence here of retirees and mining workers with health care plans and prescription cards invites exploitation of the elderly and others by illicit brokers.

There have been reports of some dealing in New Orleans. But authorities said there was no evidence of large-scale OxyContin abuse in major drug markets in New York or other urban areas. Authorities said that one mark of the new addiction was its rootedness in areas that have had no previous heavy criminal drug traffic to compete against.

Dealers shop for doctors who may be busy, slipshod or quietly cooperative, and then they obtain multiple prescriptions in several areas using the same ailing or not-so-ailing patients, police say.

For their efforts, dealers realize a tenfold profit over the painkiller's prescription cost. Addicts have been paying about $1 a milligram for the drug. The top of the line is a powerful 160-milligram tablet intended to work for up to 12 hours.

Authorities expressed little doubt that the abuse of OxyContin was spreading.

Sgt. Kerry Rowland of the Cincinnati police pharmaceutical diversion squad, said: "It's becoming the prescription drug of choice from greater Cincinnati to rural Ohio. It's become rampant because it offers such a pure high with less risk of arrest or overdose, and many times health care is picking up the cost."

He said that his squad's average arrests lately include one health care worker a week caught dealing in prescription drugs.

Another concerned area is the region surrounding Roanoke in southwestern Virginia. On Wednesday, 100 local, state and federal law enforcement officials met to discuss mounting overdoses, pharmacy break-ins and other problems associated with OxyContin abuse there, Robert Crouch, the United States attorney in Roanoke, said. "The graph is spiking," he said.
Rick Moorer, an investigator with the state medical examiner's office in Roanoke, said that in 1999 there were 16 deaths in southwestern Virginia attributable principally to OxyContin in combination with other drugs or alcohol. There was just one such death in 1997, he said.
Federal data shows that while emergency room visits involving oxycodone remained stable from 1990 to 1996, such visits doubled from 3,190 in 1996 to 6,429 in 1999, the period that corresponds with OxyContin's introduction and marketing. That data indicated that deaths attributed to oxycodone products also grew during that period. Drug company officials insisted, however, that they were not aware of any significant instances of OxyContin abuse until about a year ago when they began hearing the first media reports concerning the drug's abuse.
The new bulletin by the National Drug Intelligence Center warns that the abuse of OxyContin appears for now to be concentrated in Eastern states. But officials said that instances of abuse have surfaced as far west as California.
Chuck Miller, a spokesman for the intelligence center, said, "It's showing up elsewhere." He noted that the bulletin warned authorities that continued abuse of OxyContin was likely. Roy W. Hatfield, the police chief of Harlan, Ky., said: "In the last year, this drug has really shown up around here, pushing out all the old stuff, marijuana, barbiturates. People think it's a legal way to stay high. But now they're discovering how easy it is to get addicted."
Mr. Famularo, the United States attorney here, said his investigation would continue. "We caught 207," he said. "We didn't catch half of them; that's how pervasive this thing is."

http://www.nytimes.com/2001/02/09/health/09PILL.html?ex=982689591&ei=1&en=0f805fbe014a6345

# Exhibit 13

Business/Financial Desk; Section A

**Sales of Painkiller Grew Rapidly, But Success Brought a High Cost**

By BARRY MEIER and MELODY PETERSEN

Mar. 5, 2001
New York Times
Page 1, Column 1


Dr. Peter Leong recalls the day when he finally snapped at a drug company salesman pressing him to prescribe a powerful narcotic painkiller called OxyContin.

The drug's producer, Purdue Pharma, had already failed to persuade Dr. Leong with repeated offers of free weekend trips to Florida to discuss pain management. But when the salesman suggested that OxyContin -- which is as potent as morphine -- was safe enough to treat short-term pain, Dr. Leong exploded.

"We threw him out of my office," said Dr. Leong, who runs a pain clinic in Bangor, Me. He thinks OxyContin is potentially too dangerous to use for anything but chronic, severe pain. "OxyContin is a good drug," he said. "But the problem was, they were pushing it for everything."

If Dr. Leong was not a convert, many others were. In a little over four years, OxyContin's sales have hit $1 billion, more than even Viagra's. Although the drug has helped thousands of people in pain, its success has come at a considerable cost. An official of the Drug Enforcement Administration said no other prescription drug in the last 20 years had been illegally abused by so many people so soon after it appeared.

OxyContin has been a factor in the deaths of at least 120 people, and medical examiners are still counting, according to interviews with law enforcement officials. And doctors like Dr. Leong, pharmacists and law enforcement officials say part of the problem is that Purdue Pharma often oversold OxyContin's benefits without adequately warning of its potential for abuse.

The company also used an often criticized but increasingly common marketing strategy: currying the favor of doctors in private practice with free trips and paid speaking engagements. Purdue Pharma, based in Norwalk, Conn., paid the transportation and hotel costs for hundreds of doctors to attend weekend meetings in spots like Florida to discuss pain management, a company consultant said. Doctors were then recruited and paid fees to speak to other doctors at some of the 7,000 "pain management" seminars that Purdue sponsored around the country. Those meetings stressed the importance of aggressively treating pain with potent, long-acting painkillers like OxyContin.

Purdue also contributed to foundations supporting research on pain, to pharmacy schools and to Internet sites aimed at educating consumers.

As OxyContin's marketing message spread, the drug caught on with many doctors who medical experts said had little experience in prescribing powerful narcotics. As a result, they often could not spot those who intended to abuse the drug or who did not need it in the first place.

OxyContin, introduced in December 1995, has offered patients something different: a tablet that slowly releases its powerful pain medication, permitting patients, for example, to sleep through the night. "It's a good drug in the right situation," said Dr. Art VanZee, a physician in St. Charles, Va.

Purdue officials say they have promoted the drug responsibly and would have disciplined any sales representative who did not. They also said that in informing doctors about the drug, they told them how to spot potential drug abusers, and they have responded quickly to reports of spreading problems.

"We don't have strong medicines that don't have abuse potential," said Dr. J. David Haddox, the company's senior vice president for health policy. "What we have to do is walk the balance between helping the greater good, knowing there are always some people who will divert drugs."

Abuse and addiction involving OxyContin have spread quickly in the last two years, flaring up in at least a dozen states. And while the illegal use of OxyContin took root in rural areas along the East Coast, it has begun moving into cities like Philadelphia. "Nobody is immune from this," said Brantley Bishop, a narcotics investigator in Alabama. "I'm seeing housewives; I'm seeing loggers, nurses, mechanics."

OxyContin was originally thought to be less prone to abuse because its narcotic was locked in a time-release formula. That meant it would not produce the quick spike of euphoria that drug abusers crave. But abusers quickly discovered how to disarm the time-release formula; they simply crushed the tablet, then swallowed, inhaled or injected the powder to give themselves a high as powerful as heroin's.

Getting OxyContin was often easy. A person simply had to find the right doctor, claim great pain and get a prescription. Others just stole prescription pads and wrote their own.

Illegal use of OxyContin mushroomed even though no drug in this country is more tightly regulated. Unlike illegal drugs like cocaine or heroin, OxyContin is monitored by state and federal health officials in its production, marketing and distribution. Now, many of those regulators are trying to figure out how the outbreak occurred and what they might have done to prevent it.

The Food and Drug Administration, for one, is reassessing how it reviews prescription narcotics for potential abuse. "We've learned something from this," said Dr. Cynthia McCormick, director of the F.D.A.'s division of anesthetics, critical care and addiction drug products. Dr. McCormick acknowledged that the F.D.A. had failed to research all the ways abusers might tamper with OxyContin, an oversight she said her agency did not want to repeat.

Last Thursday, officials of five states met in Richmond, Va., to discuss ways to halt illegal traffic in OxyContin. In recent months, Purdue has also stepped up its efforts to halt the drug's abuse, including working with law enforcement officials.

Selling a 'Miracle' Drug

OxyContin came to market amid a sea change in how doctors treated pain. For years, terminally ill patients suffered needlessly because doctors resisted prescribing frequent, potent doses of narcotics, fearing that patients might become addicted.

But with new studies showing that doctors undertreated pain, OxyContin provided a breakthrough opportunity for Purdue Pharma. Until then, the company's biggest drug was MS Contin, which had limited appeal, partly because it contained morphine. OxyContin had broader appeal because it

contained a synthetic version of morphine called oxycodone, which, among other things, carried less of a social stigma.

"If Grandma is placed on morphine it's like, 'Oh, my God,' " said Dr. Howard A. Heit, a pain specialist in Fairfax, Va., and a Purdue consultant. "But if Grandma comes home placed on OxyContin -- that was O.K."

Although other pain medicine had long contained oxycodone, OxyContin differed in two key respects: it had a time-release formula, and it could be delivered in larger doses because it did not contain the type of nonprescription pain relievers that in larger quantities could cause liver damage.

The F.D.A. approved OxyContin for those with moderate to severe pain lasting more than a few days.

OxyContin is often prescribed for people in chronic pain, like those with back problems or severe arthritis, as well as patients with cancer and other painful diseases.

For Robert E. Mitchell, OxyContin proved nothing short of a wonder drug. A victim of Guillain-Barre syndrome, a rare nerve disorder that can cause paralysis, Mr. Mitchell said his pain had become so severe he could not walk. But with OxyContin, he can now wear shoes and has learned to walk again.

"To me, it's like a miracle," he said.

Seeing great potential in the drug, the company hatched an ambitious marketing plan. To reach consumers, Purdue financed an Internet site called Partners Against Pain, where OxyContin is promoted. It also contributed to groups like the American Pain Foundation, which championed the need for better pain treatment.

Still, most of Purdue's marketing dollars were aimed at doctors. In recent years, Purdue brought in 2,000 to 3,000 doctors to three-day retreats in California, Arizona and Florida, estimated Dr. Heit, the Purdue consultant. At those meetings, doctors were lectured about treating chronic pain, while being recruited to serve as paid speakers at medical meetings sponsored by Purdue.

Dr. Susan Bertrand, who treats chronic pain in Princeton, W. Va., became a Purdue speaker. She said that for her, recent studies showing the undertreatment of pain had been "almost a religious experience," making her realize how poorly she and others had been trained to deal with the problem.

To help change that, she said, she gave about a dozen paid speeches sponsored by Purdue. The company also helped her start the Appalachian Pain Foundation, an educational group on pain management.

Purdue's marketing campaign quickly began to pay big dividends, with OxyContin sales almost doubling every year, according to IMS Health, a firm that tracks drug sales. OxyContin now earns more in sales than any other narcotic. It also now accounts for 80 percent of Purdue Pharma's revenue, according to court documents filed by Purdue in connection with a patent dispute.

Some doctors and pharmacists said they were put off by the company's sales tactics.

"All companies market," said Dr. Diane Meier, a pain specialist at the Mount Sinai School of Medicine in New York. "But these people were in your face all the time."

Others criticized the way Purdue recruited doctors. "Essentially, they bought the doctors'

prescriptions," said Steve Schondelmeyer, a professor of pharmaceutical economics at the University of Minnesota. "It says to consumers that every time you paid for this drug, you sent your doctor to a nice meeting somewhere."

A Growing Concern

Purdue Pharma's critics agree that doctors must learn how to manage pain better. But Dr. Ted Parran, an associate professor at Case Western Reserve University School of Medicine in Cleveland, says doctors, in their rush to find a remedy, may have been blinded to another problem: addiction.

"Pain medicine docs are on a mission," said Dr. Parran, who teaches doctors how to use narcotics. "In the process, they tend to trivialize addiction."

In this regard, pharmacists play an important backup role for doctors. They provide the last medical defense for preventing addictive drugs from getting into the wrong hands. For instance, they can choose not to fill suspect prescriptions.

Some pharmacists said they, too, found Purdue's safety claims overblown.

John Craig, a co-owner of Hancocks Drug Store in Scottsburg, Ind., remembers a Purdue salesman walking into his pharmacy several years ago with reassurances that OxyContin was safer than other narcotics.

"They were going around to doctors promoting that this was the answer to all abuse," said Mr. Craig, but he already knew that local people were using OxyContin to get high. Since then, the abuse has become worse.

Another pharmacist, Samuel A. Okoronkwo, refused to fill an OxyContin prescription for someone he thought might be an abuser. He said a Purdue salesman suggested he could get into trouble for arbitrarily not filling prescriptions. "I told him I didn't have to fill a prescription that I didn't feel was medically necessary," he said.

Another druggist, Joseph Yates in Grundy, Va., said simply, "The problem with this drug is the company."

Purdue did not comment when asked about such anecdotes.

Concern about Purdue's marketing practices has also reached the D.E.A. An agency official said its investigators had recently interviewed doctors and druggists about their dealings with Purdue.

That official said the agency was worried that Purdue was not clearly communicating the drug's serious potential for abuse. "It may take years to repair the damage that this drug has done," said that D.E.A. official, who declined to be identified.

Told of the D.E.A. comment, Purdue responded with a statement that said in part: "In 15 years of marketing narcotic analgesics, Purdue Pharma has never been questioned by the Drug Enforcement Administration regarding our marketing practices."

In May, however, the F.D.A. did question a company advertisement for OxyContin, saying Purdue had improperly implied that OxyContin could be used to treat arthritis patients without first trying milder drugs. A company spokesman said that it disagreed with the F.D.A. but had voluntarily withdrawn the

ad.

Dr. VanZee, in St. Charles, Va., has seen the destruction the drug has caused in the valleys and small mining towns of the southwestern part of that state. He said he was treating OxyContin overdoses in youngsters he had vaccinated as infants.

In the past two years, OxyContin has been a factor in the overdose deaths of 28 people in the area, said an official of the state medical examiner's office. It is difficult to tell the precise cause of an overdose, however, because more than one drug is often involved and OxyContin's active ingredient is in other drugs.

One area clinic, the Life Center of Galax, expected to treat 20 patients in its new methadone program but must now find a way to treat 300, most of them addicted to OxyContin, a clinic official said.

To stem this abuse, Dr. VanZee said, he met last fall with Purdue representatives in a bid to persuade them to cut back on their marketing and to issue a nationwide alert about the drug's hazards. The officials, Dr. VanZee said, appeared sympathetic, but said they viewed the problem as being limited to just a few areas of the country.

"They are either very naive about the extent of the problem," Dr. VanZee said, "or they don't understand what it means to have 300 people in your county addicted -- the type of pain that causes in a community and in families."

Addressing the Problem

Purdue officials said they were as surprised as anyone that OxyContin could be abused. Dr. Haddox of Purdue said he thought the time-release formula would make the pill "less desirable to addicts."

That is not the case now. Last September, the company gathered 20 consultants to look for better ways for doctors to spot potential abusers, said Dr. Heit, the consultant. Four months later, Purdue asked its sales force to remind doctors that drugs like OxyContin "are common targets for both drug abusers and drug addicts."

Purdue said it was now planning to reformulate OxyContin, making it less appealing to abusers. The company is also helping to educate students on the dangers of prescription drugs.

Moves like this have recently earned the company praise from some law enforcement officials.

Some health officials think OxyContin abuse might have been more quickly identified had more states closely tracked the prescribing patterns of narcotics; some 17 states do that now.

Hospitals are addressing the problem in different ways. Mercy Hospital in Portland, Me., gives OxyContin patients urine screens to verify that they are not taking too much, or that they are obtaining the drug but not taking it and then selling it on the street.

A Cincinnati-based hospital chain, the Health Alliance, decided last month to limit OxyContin to just a few types of patients, like those with cancer, after determining that another painkiller was just as effective, cheaper and less prone to abuse.

Purdue Pharma -- and some doctors -- now worry that media reports on OxyContin abuse are scaring away patients who need the drug. "The publicity, of which you are a part, is causing patients to call us

in tears because their physicians are taking them off therapy," said Robin Hogen, a company spokesman. "This is becoming a sad case of patients being abused by drug abusers."

Three Founders Of Purdue Pharma

Unlike many drug companies that are publicly traded, Purdue Pharma is privately held and part of a network of concerns founded by three brothers, Arthur, Mortimer and Raymond Sackler, all of whom were trained as research psychiatrists and have illustrious ties to the arts and sciences.

A wing of the Smithsonian Institution in Washington bears the name of Dr. Arthur M. Sackler, who died in 1987. He and his brothers also financed a wing at the Metropolitan Museum of Art that houses the Temple of Dendur. In 1995, Dr. Raymond R. Sackler was knighted by Queen Elizabeth in recognition of his contributions to the sciences, arts and astronomy.

The company is now run by the son of Dr. Raymond Sackler, Dr. Richard Sackler, a surgeon who has served as a director of the foundation of the American Medical Association. A Purdue Pharma spokesman declined to make the Sackler family members available for interviews.

Medicine Merchants

Earlier articles in this series have examined the financing of a blockbuster drug, how lower-costing generic drugs can be kept off the market, alliances between drug companies and patient groups and the production of inexpensive copycat drugs in nations like India.

Articles in this series will remain available at The New York Times on the Web:

http://www.nytimes.com/drugs

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# Exhibit 14

# (Intentionally Omitted)

# Exhibit 15

**PURDUE PHARMA INC.**

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**Minutes of a Meeting**
**of the Board of Directors**

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**April 26, 2007**

A meeting of the Board of Directors of Purdue Pharma Inc., a New York corporation (the "Corporation"), as a general partner of Purdue Pharma L.P., a Delaware limited partnership (the "Partnership"), Purdue Pharmaceuticals L.P., a Delaware limited partnership ("Purdue Pharmaceuticals"), Purdue Transdermal Technologies L.P., a Delaware limited partnership ("PTT"), Purdue Pharma Products L.P., a Delaware limited partnership ("PPPLP"), DT Partners L.P., a Delaware limited partnership ("DT Partners") was held on April 26, 2007 (the "Meeting"). A quorum of the Board of Directors was present, and at the request of those Directors present, Stuart D. Baker acted as Secretary of the Meeting.

After discussion, and on motion duly made and seconded, it was unanimously decided as follows:

RESOLVED, that the revised 2007 budget for the Partnership be and the same hereby is approved in the form attached hereto as Schedule 1, which revised 2007 budget includes additional S&P expense headcount approval. Preparatory work may proceed with respect to the proposed Field Force Expansion of 100 Sales Representatives, 13 District Managers, 2 Regional Managers and 2 Administrative Support Staff; provided however, these additional 117 personnel may not be hired unless approved by the Board of Directors; and further

RESOLVED, that the Partnership be and it hereby is authorized and directed to approve the following changes effective January 1, 2008 with respect to the Purdue Health Benefit Plans:

**Redacted**



 