PURDUE

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October 10, 2003

Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. 2003N-0294 - Anesthetic and Life Support Drugs Advisory Committee Meeting - Opiate Risk Management

On September 9 and 10, 2003, the Anesthetic and Life Support Drugs Advisory Committee (ALSDAC) met to discuss Risk Management Programs (RMPs) for modified-release opiate analgesic drug products. On September 10, 2003, the committee discussed the abuse liability and Risk Management Program for Purdue Pharma L.P.'s Palladone™ (hydromorphone hydrochloride extended-release) Capsules.

With this submission, Purdue is providing responses to two issues that were raised during the discussion of the Palladone RMP, as we had discussed at the ALSDAC meeting with Dr. Nathaniel Katz, Chair of the ALSDAC.

Following our presentations, there was a question from the committee regarding the pharmacokinetics of Palladone Capsules. Purdue was asked to quantify the increase in peak plasma levels of hydromorphone between single dose administration and steady state. In error, a response was given that there was about a 20% increase. Re-examination of the data shows that depending on the study and methodology, the actual value is between 75 - 150%. With this letter, we would like to correct the misstatement.

Secondly, at several points during the ALSDAC meeting, there was discussion of the added benefit of extended-release opiate analgesics over currently marketed immediate-release products. As part of our response to this issue, we stated that there were studies that addressed this issue of various designs and lengths of treatment, and referenced a few published articles. Attached to this letter are the mentioned publications, as well as several additional examples of the kinds of published studies that are currently available:

> Caldwell, J. R.; Hale, M. E.; Boyd, R. E.; Hague, J.M.; Iwan, T.; Shi, M. and Lacouture, P.G. Treatment of osteoarthritis pain with controlled release oxycodone or fixed combination oxycodone plus acetaminophen added to nonsteroidal antiinflammatory drugs: A double blind, randomized, multicenter, placebo controlled trial. The Journal of Rheumatology 1999: 26: 862-869.

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Cheville, A.; Chen, A.; Oster, G.; McGarry, L. and Narcessian, E. A randomized trial of controlled-release oxycodone during inpatient rehabilitation following unilateral total knee arthroplasty. The Journal of Bone & Joint Surgery 2001: 83-A (4): 572-576.

Ferrell, B.; Wisdom, C.; Wenzl, C. and Brown, J. Effects of controlled-release morphine on quality of life for cancer pain. Oncology Nursing Forum 1989: 16(4): 521-526.

Haythornthwaite, J.A.; Menefee, L.A.; Quatrano-Piacentini, A.L. and Pappagallo, M. Outcome of chronic opioid therapy for non-cancer pain. Journal of Pain and Symptom Management 1998: 15: 185-194.

Miaskowski, C.; Dodd, M.J.; West, C.; Paul, S.M.; Tripathy, D.; Koo, P. and Shumacher, K. Lack of adherence with the analgesic regimen: A significant barrier to effective cancer pain management. Journal of Clinical Oncology 2001: 19: 4275-4279.

Sincerely,

Richard J. Fanelli, Ph.D.
Director
U.S. Regulatory Affairs

cc: Dr. Bob Rappaport, Director, FDA CDER, Division of Anesthetic, Critical Care and Addiction Drug Products (HFD-170)