DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-813

NOV 3 0 1999

Janssen Research Foundation
1125 Trenton-Harbourton Road
Titusville, New Jersey 08560-0200

Attention: Elizabeth M. Turek
Associate Director, Regulatory Affairs

Dear Ms. Turek:

Reference is made to FDA's Written Request for pediatric studies for Duragesic (fentanyl transdermal system) dated July 15, 1999, and to our subsequent telephone conference on October 6, 1999.

The section under *Population* has been changed as follows:

From: At least two hundred patients in total, to include a minimum of 40 patients whose prior opioid dose is appropriate for an initial patch size of 12.5 ug/h, providing adequate representation in children ≥ 2 years and < 6 years of age.

To: A minimum of one hundred and fifty patients in total providing adequate representation in children ≥ 2 years and < 6 years of age.

The section under *Clinical assessments* has been changed as follows:

From: Safety: vital signs, adverse experiences, post-treatment physical examination, laboratory assessments following drug administration, and other appropriate safety evaluations.
Therapeutic endpoints: Global Assessment of Pain treatment scale, Bieri Faces scale, and Varni-Thompson VAS scale to assess pain, Play Performance Scale, Child Health Questionnaire (CHQ), and use of rescue medication.

To: Safety: vital signs, adverse experiences, post-treatment physical examination, and other appropriate safety evaluations.
Therapeutic endpoints: VAS scale to assess pain, use of rescue medication, and/or Global Assessment of Pain treatment scale, and/or Bieri Faces scale, and/or Play Performance Scale, and/or Child Health Questionnaire (CHQ).

Reports of the studies that meet the terms of the Written Request dated July 15, 1999, as amended by this letter must be submitted to the Agency on or before December 1, 2001, in order to possibly qualify for pediatric exclusivity extension under Section 505(b) of the Act.

While not required for exclusivity, please submit any additional study reports regarding the pediatric population addressed in this Written Request, including patients with sickle cell crisis, opioid naïve patients, and any additional materials relevant to the safety database.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission "PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY" in large font, bolded type at the beginning of the cover letter of the submission. We recommend you seek a written agreement, as described in the guidance to industry *(Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act),* with FDA before developing pediatric protocols. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission "PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as a supplement to your approved NDA with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "SUBMISSION OF PEDIATRIC STUDY REPORTS - PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North 11, 7500 Standish Place, Rockville, MD 208552773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits in the pediatric patient population.

If you have any questions, call Indira Kumar, Regulatory Project Manager, at (301) 827-7410.

Sincerely yours,

John K. Jenkins, M.D., F.C.C.P.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Archival NDA 19-813; IND 24,417; IND 39,645
HFD-170/division file
HFD-170/C. McCormick
HFD-170/I. Kumar/N. Chamberlin
HFD-170/C. P. Moody
HFD-170/B. Rappaport
HFD-170/S. Hertz
HFD-170/S Doddapeneni/R Uppoor
HFD-170/T. Permutt
HFD-102/J. Jenkins/L. Ripper
HFD 2/M. Lumpkin
HFD-104/D. Murphy
HFD-6/D. Locklear
HFD-007/L. Cusumano
HFD-002/T. Crescenzi

11-29-99

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Initialed by: CGM 11-18-99 2:30pm & 5:55pm, BR 11-18-99 2:30pm & 5:50pm, SH 11-18-99 2:30pm & 4:54pm
Final: C. Schumaker 11-24-99 3:00pm, 11-26-99
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REVISED PEDIATRIC WRITTEN REQUEST LETTER
INFORMATION REQUEST (IR)