IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Roychowdhury *et al.*	Customer No.	:	62965
Appln. No.	:	13/541,524	Confirmation No.	:	8238
Filed	:	July 3, 2012	Art Unit	:	1629
Examiner	:	Polansky, Gregg			
For	:	DEXMEDETOMIDINE PREMIX FORMULATION			

DECLARATION UNDER 37 C.F.R. §1.132

I, Huailiang Wu, Ph.D., hereby declare the following:

1. I am currently employed as a Group Leader, Global Pharma Research & Development, by HOSPIRA, INC., (hereafter "Hospira") having its principal place of business at 275 North Field Drive, Lake Forest, IL 60045. My curriculum vitae is attached as Exhibit A.

2. HOSPIRA, INC. is the sole Assignee of United States Patent Application Serial No. 13/541,524 (hereafter "the '524 application") pursuant to the Assignment recorded at Reel/Frame: 027480/0592 which was recorded with the United States Patent and Trademark Office (hereafter, "USPTO") on January 4, 2012.

3. I, along with other scientists employed by, and under the direction of, Hospira, designed and conducted assays relating to a ready to use liquid pharmaceutical composition for parenteral administration to a subject, comprising dexmedetomidine

or a pharmaceutically acceptable salt thereof at a concentration of about 0.005 to about 50 µg/mL disposed within a sealed glass container. Ready to use parenteral pharmaceutical compositions, such as the claimed dexmedetomidine composition, are manufactured to be sterile so that the compositions are safe to be administered to patients upon removal from their storage container. Sterility can be achieved, for example, by autoclaving the ready to use composition.

4. A first assay (Assay 1) measured the potency of various concentrations of a ready to use dexmedetomidine composition stored in Polyvinyl chloride (PVC) bags and glass vials over a three-day period following autoclave. A second assay (Assay 2) was conducted to measure the potency of various concentrations of a ready to use dexmedetomidine composition without autoclave following storage at ambient temperature over a 24 hour period.

5. As described in greater detail below, Exhibit B (describing the results of Assay 1) demonstrates an unexpected maintenance of potency of 1, 10, 15 and 50 µg/mL dexmedetomidine compositions following autoclave and storage over a three-day period in glass containers compared to storage in PVC plastic containers.

6. Exhibit C (describing the results of Assay 2) demonstrates an unexpected maintenance of potency of 1, 10, 15 and 50 µg/mL dexmedetomidine compositions when stored at ambient temperature over a 24-hour storage period without autoclave in glass containers compared to storage in PVC plastic containers.

7. For Assay 1, ready to use dexmedetomidine solutions were prepared at concentrations of 1 μg/mL, 10 μg/mL, 15 μg/mL and 50 μg/mL by dissolving dexmedetomidine and sodium chloride in water to achieve the target dexmedetomidine concentration and a 0.9% sodium chloride concentration. The solutions were then filtered through a 0.22 μm filter. A sample of the filtered solution was collected and used as the control. The filtered solution was then disposed into 100-mL PVC bags and 50-mL glass vials. The solutions from two PVC bags or two glass vials were tested for dexmedetomidine potency as the "preTS" (pre terminal sterilization) sample about 12 hours after the solutions were disposed into the PVC bags or glass vials. The remaining filled PVC bags and glass vials were autoclaved (terminal sterilization) about 12 hours after the solutions were disposed into the PVC bags or glass vials. The solutions from two PVC bags or two glass vials immediately after autoclave were tested for dexmedetomidine potency as the "T=0" samples. The autoclaved PVC bags and glass vials were stored in stability chambers under conditions of 25°C/60%RH (relative humidity) and 40°C/75%RH for up to two weeks. Samples from the PVC bags and glass vials were tested after storage times of 3 days, 1 week and 2 weeks (for PVC samples only). Testing to determine dexmedetomidine potency in the samples was conducted using HPLC.

8. As shown in Exhibit B, the potency of the 1 μg/mL dexmedetomidine formulation decreased by 1.82% about 12 hours after being disposed in a PVC storage bag

(preTS), and by 7.81% following autoclave (T=0) compared to control. After storage for three days in the PVC bag at 25°C and 40°C, the potency of the 1 µg/mL formulation decreased by 8.05% and 8.83%, respectively, compared to control. Similarly, the potency of the 10, 15 and 50 µg/mL formulations disposed in PVC bags decreased by 5.84%, 5.54% and 4.32% following autoclave, respectively, compared to control. After storage for three days in PVC bags at 25°C, the potency of the three concentrations decreased by 6.24%, 6.17% and 5.26%, respectively, compared to control. After storage for three days in PVC bags at 40°C, the potency of the three concentrations decreased by 6.28%, 6.62% and 5.36%, respectively, compared to control.

9. As described by Exhibit B, in contrast to storing the dexmedetomidine compositions in PVC bags, when the dexmedetomidine compositions were stored in glass vials, the potency of the dexmedetomidine was maintained. When stored in glass vials, none of the four concentrations of dexmedetomidine experienced any loss in potency after disposing the formulations in glass vials or after autoclave, compared to control. After storage for three days in glass vials at 25°C, the decrease in potency of the 1, 10, 15 and 50 µg/mL dexmedetomidine compositions were 0%, 0%, 0.39% and 0.44%, respectively, compared to control. After storage for three days in glass vials at 40°C, the decrease in potency of the 1, 10, 15 and 50 µg/mL dexmedetomidine compositions were 0.42%, 0%, 0.27% and 0.51%, respectively, compared to control.

10. As described by Exhibit B, storing a ready to use formulation of dexmedetomidine at concentrations recited by the claims of the '524 application in glass containers resulted in an unexpected reduction in potency loss of the composition compared to storage in plastic PVC containers. Storing the formulations in PVC containers resulted in a decrease in dexmedetomidine potency after disposition within the containers, after autoclave, and after a three-day storage period at 25°C or 40°C. The maximum detectable loss in potency of the samples stored in PVC containers after the three-day storage period was 8.83%, whereas the glass containers showed a maximum loss of only 0.51%.

11. For Assay 2, dexmedetomidine solutions were prepared as described for Assay 1 at concentrations of 1, 10, 15 and 50 µg/mL. A sample of the filtered solution was collected and used as the control. Prior to storage, the solutions from PVC bags and glass vials were tested for dexmedetomidine potency as the "T=0" sample. PVC bags and glass vials were stored at ambient temperature on a laboratory bench for 24 hours. Samples from the PVC bags and glass vials were tested after storage times of 12 hours and 24 hours. Testing to determine dexmedetomidine potency in the samples was conducted using HPLC.

12. As shown in Exhibit C, when stored in PVC bags, the potency of the 1, 10, 15 and 50 µg/mL dexmedetomidine compositions decreased by 1.48%, 1.22%, 1.06% and 1.78%, respectively, compared to control following the 24-hour storage period. In

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