# Stability of 20, 40 and 50 mcg/mL Fentanyl Solutions Stored in Syringes at Room Temperature (23$^0$C).

Vera Riss, Roxanne Hook, Ashleigh Neault , Erica Scharrer, Shirley Law and Scott E. Walker.

*Departments of Pharmacy, Hospital for Sick Children and Sunnybrook Health Sciences Centre, and the Faculty of Pharmacy, University of Toronto, Toronto, Ontario.*

## INTRODUCTION

Inpatient hospital pharmacies must compound intravenous products and assign an appropriate beyond-use-date (BUD) as per NAPRA standards, when products are not commercially available. Furthermore, having medications in a Ready-To-Administer format on nursing units is important for safe and timely administration.

A previous poster presentation reported the stability of 10 mcg/mL and 50 mcg/mL fentanyl solutions in CADD® Reservoirs, PVC containers and Ethylene/Propylene Co-Polymer (PAB®) bags during storage under refrigeration (4$^o$C) and room temperature (23$^0$C) for 90 days. [*Law et al. 2017; http://metrodis.org/SB_PPC.html*]

A previous publication has demonstrated the stability of undiluted fentanyl (50 mcg/mL) in polypropylene syringes and PVC bags when stored at either 5$^0$C or 22$^0$C for 28 days [*Donnelly. Intern J Pharm Compound 2005*].

Paediatric patients require lower concentrations of opioid continuous infusions than adults and while previous publications have demonstrated the stability of fentanyl, data for lower concentrations stored in syringes beyond 28 days has not been reported.

## OBJECTIVES

The objective of this study was to evaluate the stability of fentanyl concentrations of 20 mcg/mL, 40 mcg/mL and 50 mcg/mL in polypropylene syringes over a 90 day storage period at room temperature.

The concentration of fentanyl was evaluated during storage using a validated, stability indicating, liquid chromatographic method using UV detection.

Interested in a copy of this poster or other Sunnybrook Posters?

Scan the QR code or go to : http://metrodis.org/SB_PPC
And download the poster from this site.

NONE of the authors of this poster have any personal or financial relationships with any commercial entities that may have a direct or indirect interest in the subject matter of this presentation.
The fentanyl and polypropylene syringes used in this study were purchased by the Department of Pharmacy, Hospital for Sick Children.

### Liquid Chromatographic Method

The liquid chromatographic system consisted of a mixture of 28% acetonitrile and 72% 0.05 mol/L phosphoric acid which was pumped through a 15 cm x 4.6 mm reverse-phase C18, 3-µm column (Supelcosil ABZ-plus; Supelco, Toronto, Ontario) at 1.0 mL/min. The effluent was monitored at 220 nm.

### Assay Validation

A chromatographic separation was developed and evaluated to ensure reproducibility, accuracy and assay specificity. The system was shown to be capable of separating fentanyl from its degradation products and other narcotics (Figure 1). Accuracy and reproducibility of standard curves was tested over 5 days. Inter and intra-day errors of reproducibility were assessed by the coefficients of variation and the standard deviation of regression.

### Stability Study

On study day 0, 50 mL solutions of 20 mcg/mL, 40 mcg/mL of fentanyl diluted with 0.9% sodium chloride injection and 50 mcg/mL was added polypropylene Becton-Dickinson syringes. Three syringes for each concentration were stored at room temperature. Concentration and physical inspection were completed on days 0, 1, 3, 7, 14, 24, 38, 57, 77, and 90.

### Data Reduction and Statistical Analysis

Chemical stability was based on the intersection of the lower limit of the 95% confidence interval of the observed degradation rate and the time to achieve 90% of the initial concentration. Analysis of variance was used to test differences in degradation rate.

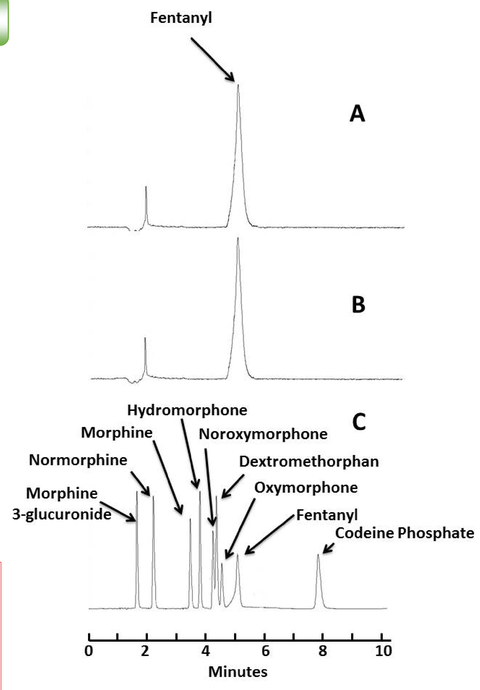


**Figure 1.**
Chromatogram A represents a 50 mcg/mL fentanyl solution in a polypropylene syringe on study day zero.
Chromatogram B represents the same 50 mcg/mL fentanyl solution in a polypropylene syringe following storage for 90 days at room temperature.
Chromatogram C represents a mixture of various narcotics demonstrating the ability of the chromatographic system to separate similar compounds. Fentanyl elutes at 5 minutes and is separated from all other compounds.

Note. After 90 days of storage at room temperature *additional peaks are not present* in the chromatogram indicating the lack of observed degradation of fentanyl during storage .

## CONCLUSIONS

This study has demonstrated that concentrations of 20 mcg/mL and 40 mcg/mL (diluted in saline) and with undiluted fentanyl in polypropylene syringes retain more than 96% of the initial concentration, with 95% confidence, over the 90-day study period.

As with previously reported studies of fentanyl in both PVC bags and polypropylene syringes, a clinically unimportant degree of change in concentrations was observed.

The results of this study demonstrate extended chemical stability of fentanyl admixtures, exceeding USP General Chapter <797> BUD limits.

When establishing a BUD in your institution, consideration of the sterile compounding environment and sterility testing of the final product , must be considered.

## RESULTS

### Concentration Results

Concentrations on each study day are reported in Table 1 and were observed to deviate by less than 3% over the study period (90 days) when stored at room temperature.

The calculated use-before-date, with 95% confidence, averaged 263 days, exceeding the 90-day storage period for all concentrations.

### Assay Validation

Assay validation demonstrated that numerous other narcotics are separated from fentanyl (Figure 1). Standards and quality control samples over the study period showed an average absolute deviation of 2.46% from the expected concentration. Analytical error with replicate measurement (as measured by coefficient of variation) averaged 0.58% within a day and 1.40% between days. A second estimate of between days analytical error, as measured by the standard deviation of regression averaged 0.50%.

Analysis of variance revealed significant differences in percent remaining due to study day ($p < 0.001$), and concentration ( $p < 0.001$). The study was capable of detecting a 0.42% difference in concentration due to study day and concentration or container. The difference due to concentration is about 1% and may be unimportant.

### Table 1. Percent Remaining of the Initial Fentanyl Concentration.

| | | Syringe RT 20 mcg/mL | Syringe RT 40 mcg/mL | Syringe RT 50 mcg/mL |
|---|---|---|---|---|
| Study Day | Initial concentration (mcg/mL) | 19.46±0.68 | 39.68±0.27 | 49.44±0.57 |
| 1 | | 100.37±0.27 | 100.07±0.09 | 99.61±0.52 |
| 3 | | 101.07±1.03 | 99.78±0.59 | 99.42±0.61 |
| 7 | | 100.91±0.87 | 98.87±0.42 | 99.39±0.53 |
| 14 | | 99.75±0.15 | 98.54±0.53 | 99.33±0.46 |
| 24 | | 99.78±0.77 | 98.00±0.47 | 98.70±0.57 |
| 38 | | 99.19±0.38 | 99.52±1.39 | 99.01±0.54 |
| 57 | | 99.37±0.66 | 98.41±1.98 | 98.35±1.19 |
| 77 | | 98.33±0.64 | 97.11±1.51 | 96.68±0.07 |
| 90 | | 98.81±1.15 | 97.20±1.70 | 97.38±0.99 |
| | Degradation rate (%/day) [Slope] | -0.023 | -0.027 | -0.030 |
| | Intercept (Percent of Initial Concentration) | 100.47 | 99.61 | 99.71 |
| | Correlation coefficient (r) | -0.864 | -0.832 | -0.938 |
| | Standard Deviation of Regression (Sy.x) | 0.467 | 0.644 | 0.387 |
| | Standard Error in Slope (Sb) | 0.0047 | 0.0065 | 0.0039 |
| | Confidence Interval for slope | 0.0108 | 0.0149 | 0.0090 |
| | Fastest Degradation Rate - 95% Confidence | -0.0337 | -0.0424 | -0.0387 |
| | Shortest Time to Achieve 90% of Initial (T-90) - 95% CI (days) | 296.77 | 235.79 | 258.73 |