

## Introduction

Dose-banding<sup>1</sup> requires an extended shelf-life (1 - 3 months) of pre-made drug infusions. This study evaluated the chemical and physical stability of oxaliplatin infusions using a sequential temperature cycling design. This design challenges physical stability and support the re-issue of infusions in cases of treatment delays.

## Preparation of oxaliplatin infusion bags

- ▶ 7 groups of oxaliplatin infusion bags (Group A, B, C, D, E, F, G) were prepared with 5% glucose.
- ▶ Each group comprised of:
  - ▶ 3 × 0.2mg/ml infusion bag
  - ▶ 3 × 0.7mg/ml infusion bag
- ▶ All infusion bags were protected from light.

## HPLC method for chemical stability test

A bonded-phase cyano column of Water Spherisorb (CNRP) was used to separate oxaliplatin in a HPLC method which was stability-indicating and fully validated for this particular study.

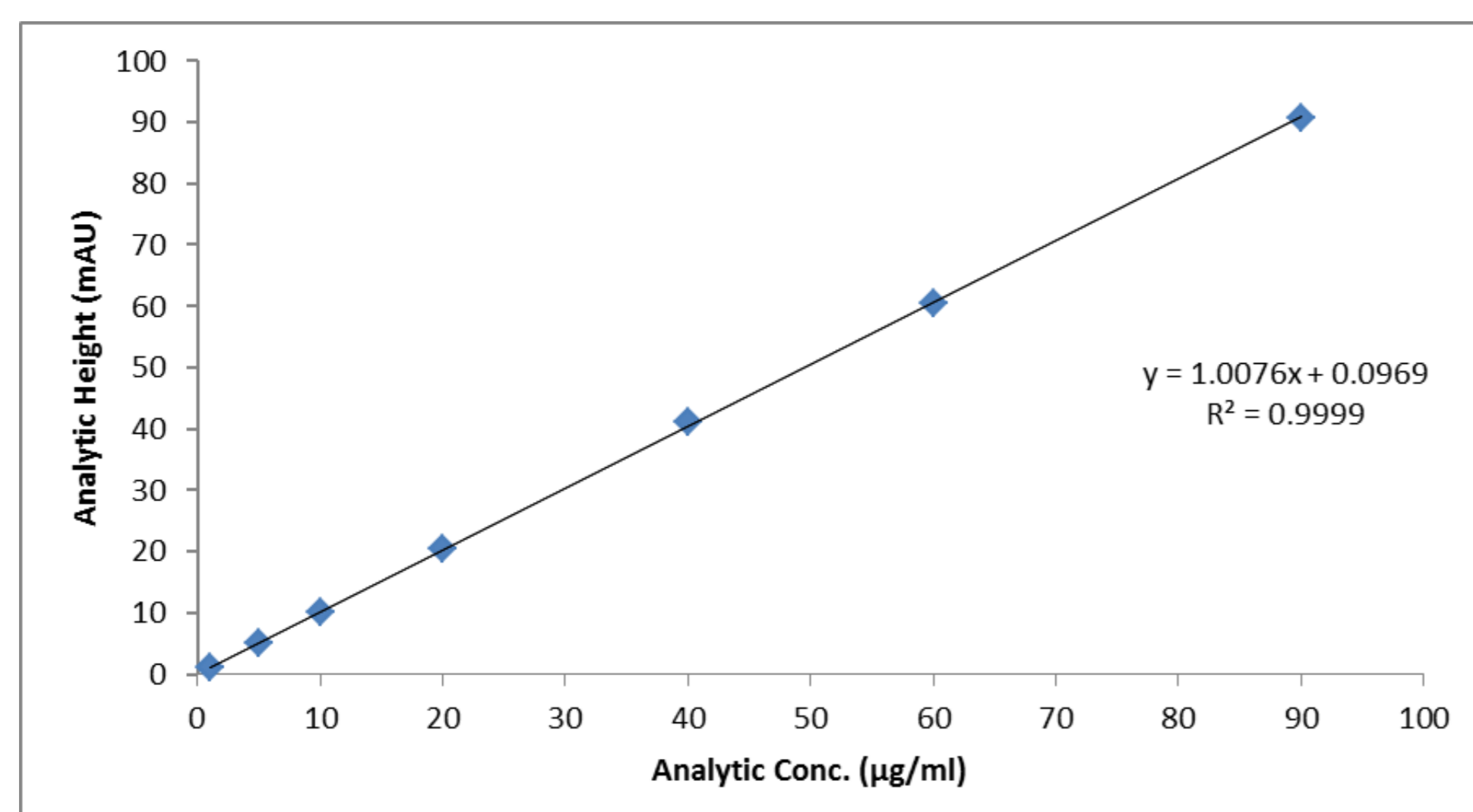


Figure 1 : Oxaliplatin calibration plot over the concentration range of 1.0 – 90.0 µg/ml (n = 7).

## Physical stability evaluation

Physical stability of oxaliplatin infusions was evaluated as shown in Figure 2.

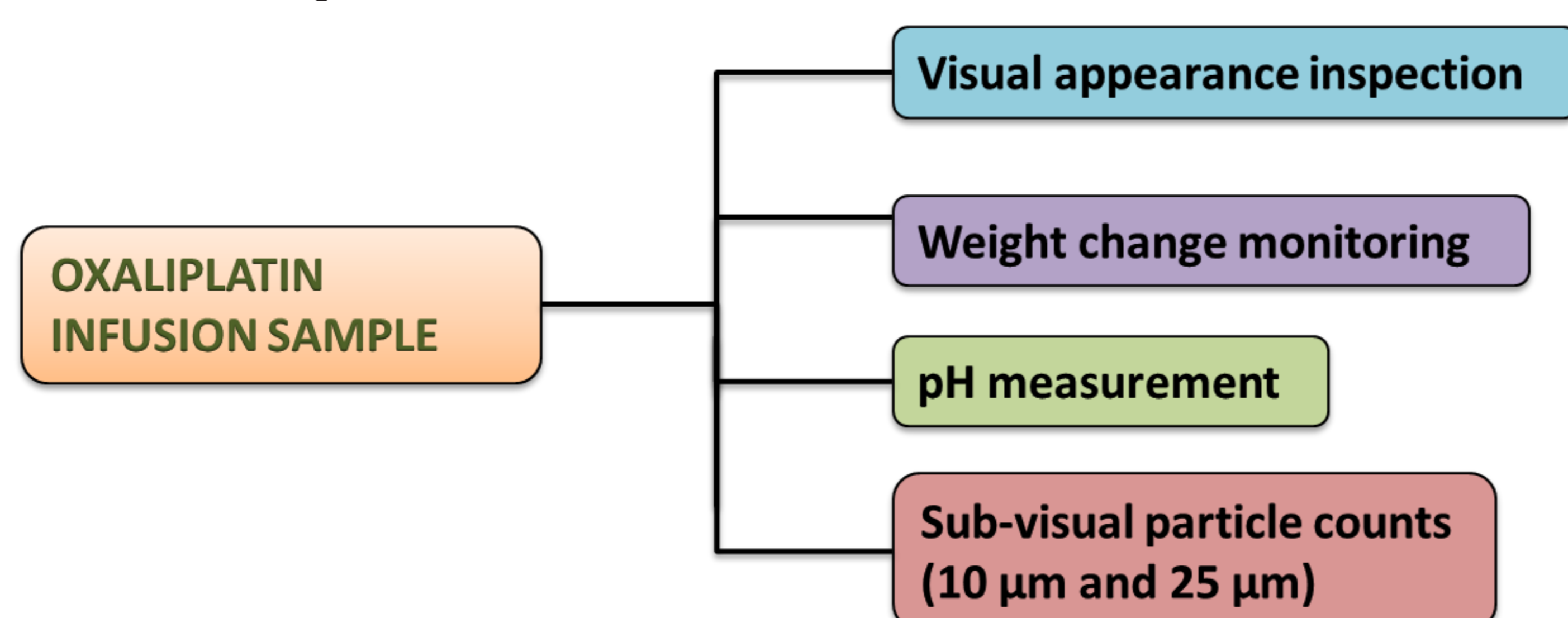


Figure 2 : Physical stability tests for oxaliplatin infusion samples.

## Conclusion

This rigorous study extends the known shelf-life of oxaliplatin infusions and facilitates an oxaliplatin dose-banding scheme. Oxaliplatin infusions, stored for 84 days at 2 – 8°C, remained stable after incubation of 24 hours at 25°C and a further 7 days at 2 – 8°C, replicating re-use of infusions after treatment delay.

<sup>1</sup> Plumridge, R J & Sewell, G J, Dose-banding of cytotoxic drugs: A new concept in cancer chemotherapy, *Am J Health-Syst Pharm*, 58,(18), pp 1760-1764, 2001.

## Sequential temperature cycling protocol

The sequential temperature cycling scheme is shown below.

- ▶ Step 1: Storage at 2 – 8°C (refrigerated temperature).
- ▶ Step 2: Incubation at 25°C (room temperature).
- ▶ Step 3: Storage at 2 – 8°C after step 2.

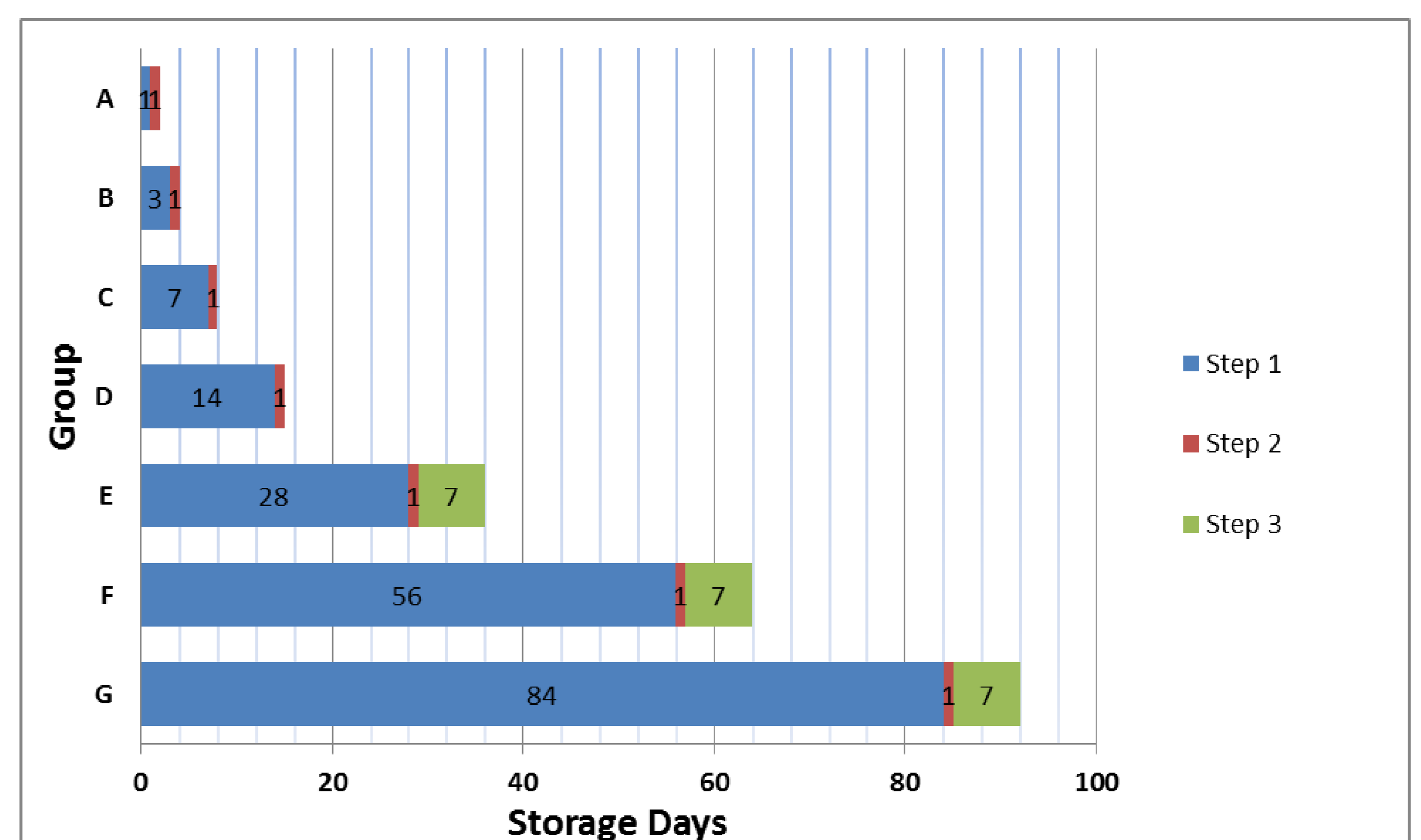


Figure 3 : Graphical summary of the study process for oxaliplatin infusion groups (Group A - G) with the sequential temperature cycling storage conditions.

Samples were analysed at the end of each step to determine chemical and physical stability.

## Result and Discussion

- ▶ Oxaliplatin infusions at both concentrations were chemically (95 – 105% of initial concentration) and physically (no significant change) stable throughout the entire study.
- ▶ The extended shelf-life (84 days at 2 – 8°C) of oxaliplatin infusions can support the advance batch preparation of standard infusions required for dose-banding.
- ▶ The ability to re-refrigerate the infusions for up to 7 days following 24 hours exposure to room temperature will reduce infusion wastage in cases where treatment is delayed for clinical reasons.