Semi-automated potency assay with increased consistency and less hands-on time (case study)

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INTRODUCTION

For quality control (QC) of biopharmaceuticals, cell-based assays (CBA) and/or binding assays are required for batch release and stability assessment. A typical CBA exhibits intrinsic variability influenced by factors such as the number of pipetting steps, assay complexity, analyst experience, and the use of living cells, unlike ELISA or SPR binding assays.
Although full assay automation has been increasingly adopted in recent years, it remains a significant challenge, particularly for QC release assays in a GMP environment. Therefore, we aimed to achieve semi-automation in a modular manner, as potency assays can be divided into smaller steps, facilitating the selective automation of specific parts of the assay.
Here, we share our experience with various implementations of Integra automation systems to enhance the reproducibility of assays, streamline workflows, and minimize hands-on time for analysts.

RESULTS

Principle of cAMP Hunter™ Tirzepatide Bioassay Kit

A bioassay for Tirzepatide was developed using cAMP Hunter™ Bioassay Kit from Eurofins DiscoverX (Fig. 1).

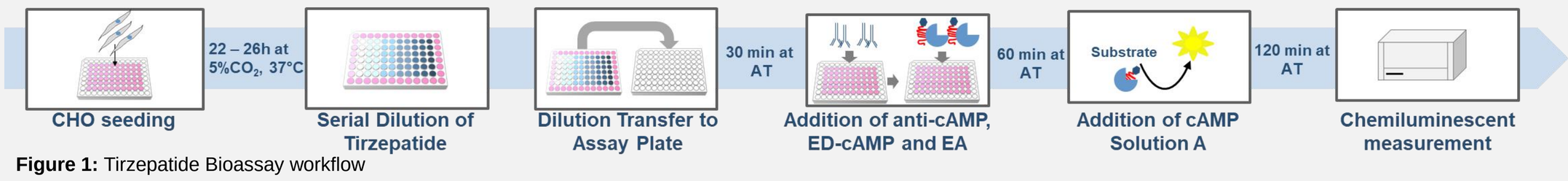

Figure 1: Tirzepatide Bioassay workflow

Initial assay performance (manual)

Tirzepatide Bioassay was performed acc. to kit manual. Representative dose response curves are depicted in Fig. 2.

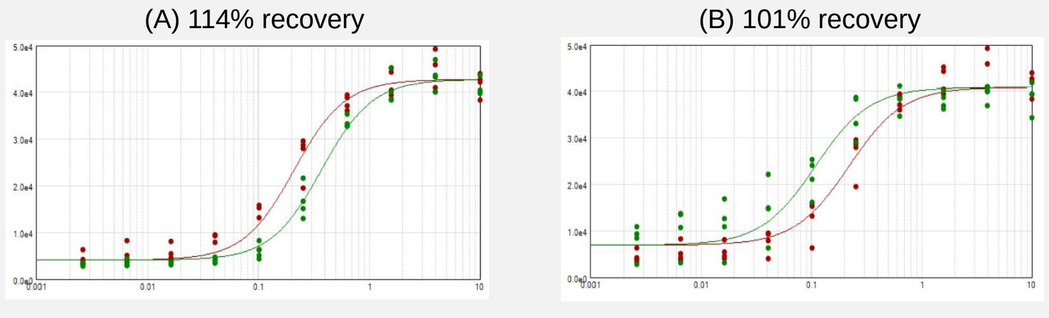

Figure 2: Representative dose response curve of the reference standard and reference standard at 50% (A) and 200% (B) expected potency performed manually.

Initial assay performance (automated)

Pipetting robots were purchased from INTEGRA Biosciences (model: ASSIST PLUS, see Fig. 3) equipped with various volumetric pipettes. The system was categorized as class B as per USP <1058> and was released for GMP.

Initially, All method steps, including cell seeding, dilution preparation, transfer, and detection reagent steps were programmed using Integra VIALAB software and transferred to the pipettes. As depicted in Figure 4 semi-automation resulted in a significant curve shift and increased variability.

Figure 3: Integra ASSIST PLUS.

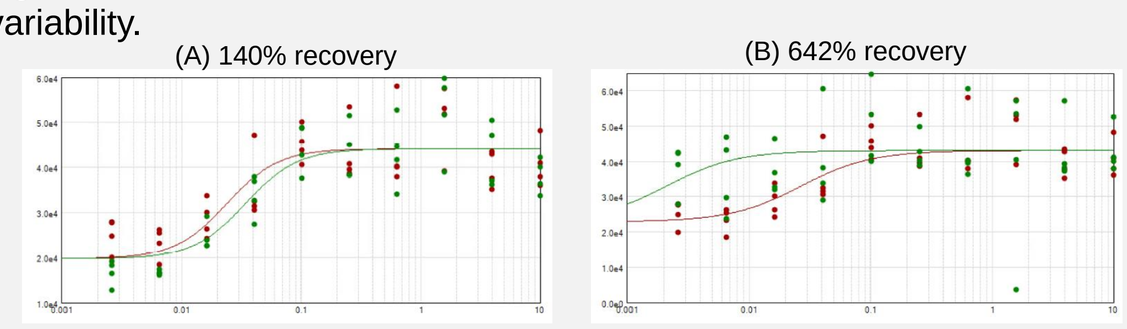

Figure 4: Representative dose response curve of the reference standard and reference standard at 50% (A) and 200% (B) expected potency performed semi-automated.

Hypothesis-driven optimization (automated)

Re-evaluation of the programming steps and pipetting times identified slow detection reagent addition as the most likely cause. To address this, two plates were run in parallel: H1: performed manually (pink) at a faster rate, while H2 was processed using a slower automated method (blue). While curve shape and variability improved, the results also revealed differences in assay windows (Figure 5).

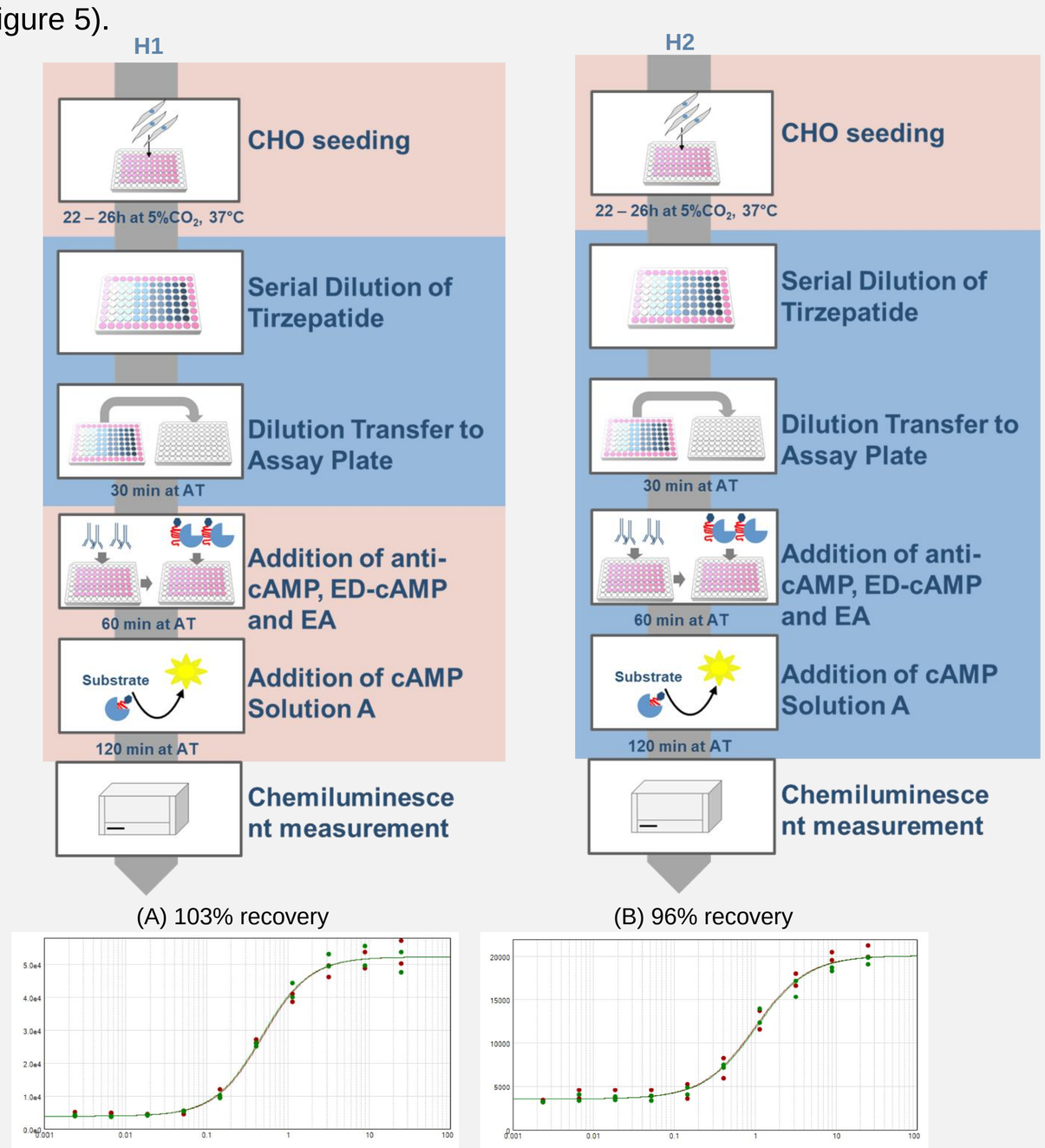

Figure 5: Dose response curve of the reference standard and reference standard at 100% expected potency performed (A) manually and (B) semi-automated. Pink: manual steps. Blue: automated steps.

CONCLUSION

The INTEGRA ASSIST PLUS pipetting robot and Integra VIALAB software improved the semi-automation of the bioassay workflow, including cell seeding and reagent steps. Initial results showed curve shifts and increased variability, likely due to slow reagent addition. Compared to the initial method setup, the current automated solutions significantly improved assay performance and decreased hands-on time for analysts. Optimizing pipetting times and comparing addition methods improved curve shape and variability, though differences in assay windows highlighted the need for careful optimization in semi-automation for QC workflows.

RECOMMENDATION

Based on our experience, modular semi-automation for QC potency assays improves assay consistency and reduces analyst hands-on time, offering several advantages over to traditional single, 8- or 12-channel pipettes.