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Protein Titer Capabilities – A Comparison of the Cydem VT System to Current Technology across Various CHO Media

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Introduction

The Cydem VT Automated Clone Screening system sets a new standard in titer measurements, offering daily, automated cell health and titer measurements from the same sample. The Cydem VT system provides researchers with comprehensive information on antibody production, as well as crucial data on viability and growth. This integrated approach offers a holistic view of cell culture performance, enabling researchers to make well-informed decisions throughout the development process.

One of the key features of the Cydem VT system is its utilization of the fluorescence polarization detection method coupled with the technology of the Valita Titer plates. This highly sensitive assay provides reliable measurements, allowing for precise quantification of protein. By leveraging this advanced IgG detection method within the titer module combined with the trusted technology of the Vi-CELL BLU analyzer in the cell health module, the Cydem VT system ensures the collection of reproducible data, enhancing the overall quality of research.

Moreover, the Cydem VT system streamlines the process of titer data collection by automating the entire workflow within a single system that cultures clones and simultaneously measures viability and antibody production in the same sample. This automation not only saves valuable time by reducing hands-on interaction, but also increases the confidence in the clone-ranking process by reducing the risk of selecting bad clones or missing out on good ones. With the Cydem VT system, scientists can focus their efforts on other important tasks while titer data is being automatically collected and analyzed.

IgG quantification is critical in the clone-ranking process for cell line development (CLD). This application note aims to demonstrate the performance of the Cydem VT system in comparison to a widely used immunoturbidimetric detection method for IgG quantification. To achieve this, samples were analyzed using both the Cydem VT system and the reference immunoturbidimetric system.

This study highlights the linearity and comparability of the Cydem VT system against the reference device, highlighting its potential advantages over a common traditional method in IgG quantification and clone ranking.

Methods

In order to demonstrate how the Cydem VT system compares to current protein detection systems commonly used in the clone-ranking process, samples were run on the Cydem VT system and compared to a popular system utilizing an immunoturbidimetric detection method for IgG quantification.

To test linearity across the IgG range compared to an offline analysis device for reference, a 10-point concentration series was prepared for this study using Beckman Coulter IgG Standard diluted with ActiPro media and tested both online and offline. The Cydem VT system normally utilizes an automatic dilution method, starting with no dilution (1x) and increasing to 2x, 5x, and 10x dilutions as more IgG is produced within the well. To demonstrate dilutional linearity, certain concentrations falling within overlapping ranges of each dilution were tested with both dilutions:

For the comparative analysis, the 10 different IgG solutions were measured in parallel using both the Cydem VT system and the reference immunoturbidimetric system. Solution with concentrations falling into the overlap region of the dilution ranges on the reference device were also run using both the standard and high dilution options.

To normalize the measurements between the two systems, the Beckman Coulter IgG Standard was diluted with ActiPro media to create an expected concentration of 1100 mg/L based on the assay sheet value. This concentration was run on the reference system and determined to be a concentration of 994 mg/L. This value was used as the input concentration for the Cydem VT standard curve. Since this IgG was known to have moderate binding affinity to the probe used in the titer plates, a specimen volume of 10 QL was used, as shown below:

To further validate the titer module's performance across different media conditions commonly used in bioprocessing, the same methodology was applied using Freestyle CHO, BalanCD CHO, and PowerCHO 2 media. Each media type was tested across the full IgG range (0-10 g/L) using an identical 10-point concentration series preparation method.

Additionally, to demonstrate that clone-ranking is the same using the immunoturbidimetric reference device, a 14-day fed-batch process with ActiPro media was conducted with 10 different clones with 9 to 10 replicates per clone. IgG was measured on days 9 and 14 online using the Cydem VT system and offline by generating a sample output plate, which was then analyzed using the reference immunoturbidimetric system. The IgG concentrations measured by the Cydem VT system and the offline system were compared to determine the correlation.

Point	Relative Concentration	Expected Concentration (mg/L)	Dilution Factor
10	1	8574.70	10
9	0.7841	6723.42	10
8	0.5	4287.35	10
7	0.392	3361.28	10 & 5
6	0.25	2143.68	5
5	0.1563	1340.23	5 & 2
4	0.125	1071.84	2
3	0.0781	669.68	2 & 1
2	0.0625	535.92	1
1	0.0256	219.51	1

Table 1. Expected concentrations of the 10-point dilution series and the dilution factor at which each concentration was tested. Expected concentration was calculated by taking the average measured concentration between 10 replicates of relative concentration (RC) 1, then multiplied by the RC value of each subsequent concentration to give the expected IgG concentration of each point in the dilution series.

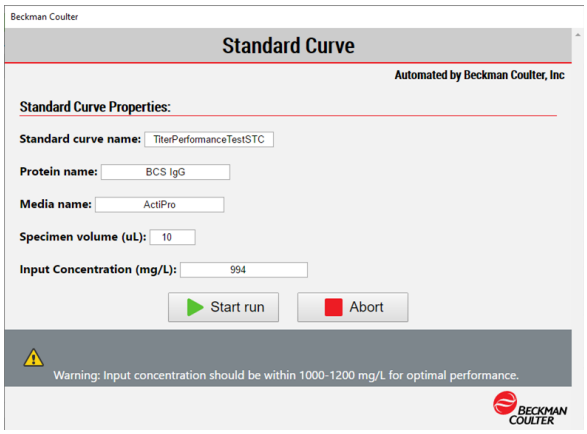

Figure 1. Standard curve input display screen. The standard curve stock concentration was determined to be 994 mg/L on the offline reference device, so in order to normalize the measurements, it was used as the input concentration for the Cydem VT system.

Results

The Cydem VT system showed linearity across the tested concentration range using ActiPro media, showing a strong correlation with the reference immunoturbidimetric system (figure 2). Furthermore, concentrations within overlapping dilution ranges confirmed the system's accuracy and reliability across dilutions (figure 3). Similar linearity and performance was demonstrated when validating the system with Freestyle CHO, BalanCD CHO, and PowerCHO media types. Each media type was tested across the full IgG range (0-10 g/L) using the same 10-point concentration series methodology, confirming the robustness of the Cydem VT system's measurements across commonly used bioprocessing media formulations (figure 4).

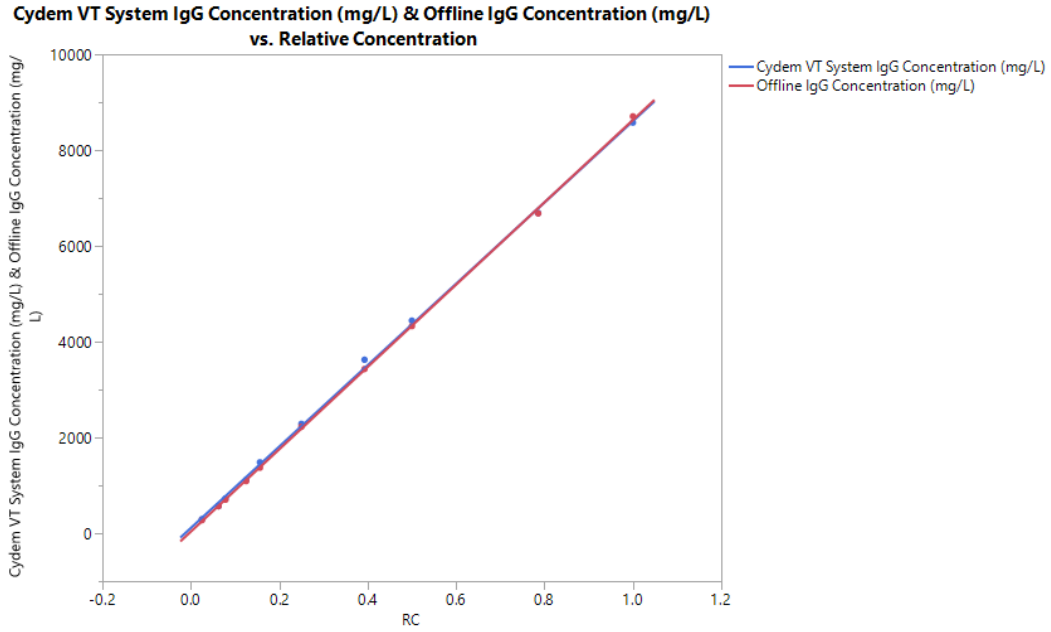

Figure 2. Comparison of the Cydem VT system IgG measurements versus the offline immunoturbidimetric system using a series of IgG concentrations generated with ActiPro media. Replicates from each concentration were averaged on both systems.

Point	Relative Concentration	Online Measurement Average (mg/L)	Offline Measurement Average (mg/L)	% Difference ([Online-Offline]/ Offline * 100)
10	1	8574.70	8706.00	-1.51
9	0.7841	6688.13	6679.67	0.13
8	0.5	4441.60	4326.00	2.67
7	0.392	3624.97	3430.00	5.68
6	0.25	2286.60	2226.67	2.69
5	0.1563	1483.72	1371.28	8.20
4	0.125	1113.55	1089.93	2.17
3	0.0781	726.47	701.77	3.52
2	0.0625	568.73	567.09	0.29
1	0.0256	296.24	274.01	8.11

Table 2. Average measured values from the Cydem VT system to the reference system. Note: the RC 1 value was out of range for the reference system, so was diluted 1:1 with ActiPro media in order to obtain the concentration.

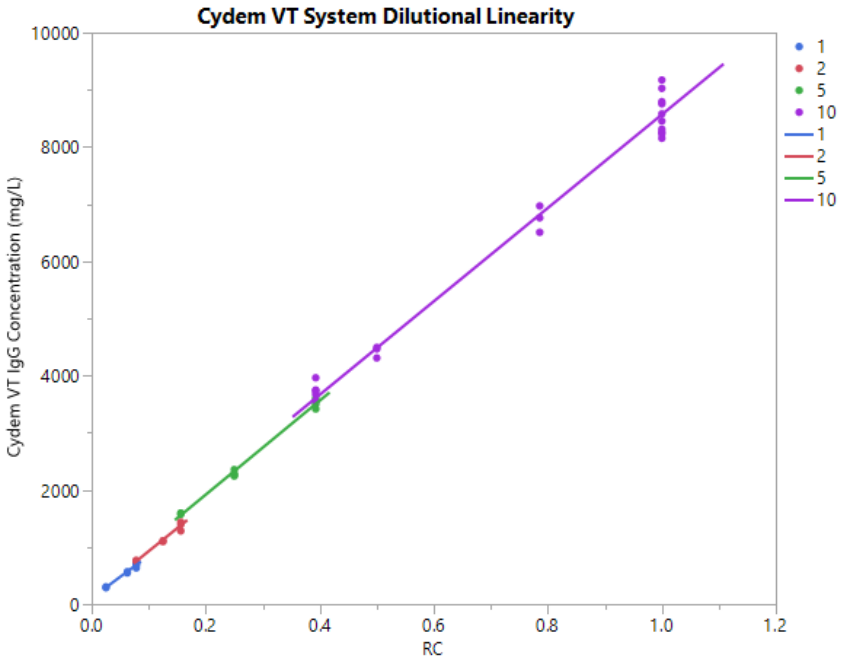

Figure 3. Linearity of the Cydem VT system across dilution ranges (1x, 2x, 5x, and 10x dilutions).

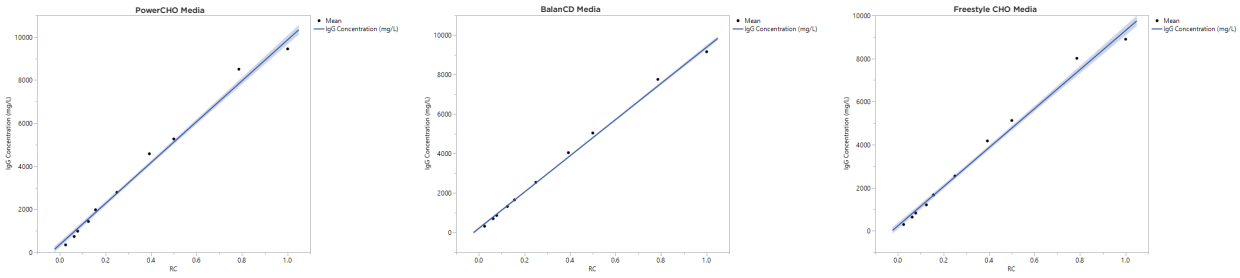

Figure 4. Linearity of the Cydem VT system antibody titer measurements across 3 different media types.

The 14-day fed-batch process results further demonstrated instrument comparability, as the clone rankings obtained from the Cydem VT system were consistent with those from the offline reference device (figure 5). The titer concentrations measured online were comparable to those measured offline with an R2 value of 0.972, supporting the reliability of the Cydem VT system for clone ranking.

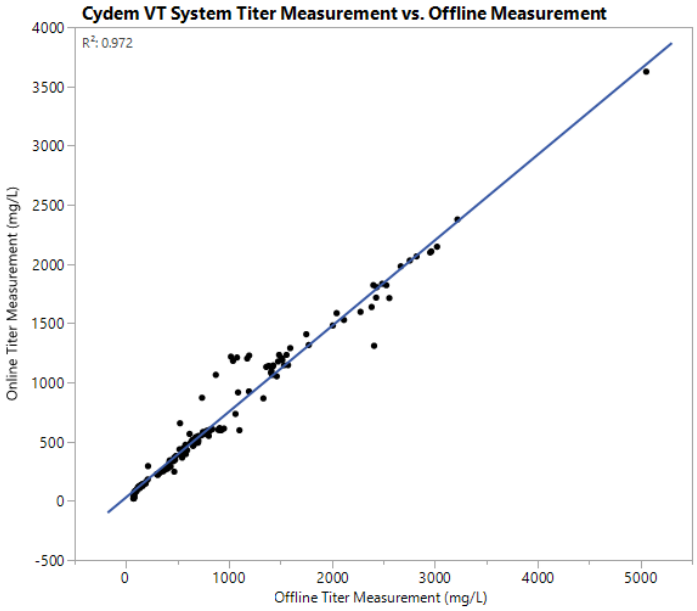

Figure 5. Correlation of titer measurements from the 10-clone fed-batch culture run on the Cydem VT system to the turbidimetric assay offline reference device on days 9 and 14 of the 14-day fed batch campaign. Some measurements had exceeded the upper limit of detection for the dilution range used, which reported a "null" value. These measurements were excluded from analysis.

Discussion

The findings from this study demonstrate titer measurement comparability by the Cydem VT Automated Clone Screening System to a reference instrument in the realm of antibody measurements. The system not only closely correlates with offline IgG measurements traditionally provided by immunoturbidimetric detection methods, but also enhances the efficiency of obtaining results by allowing for automated sampling.

One of the standout features of the Cydem VT system is its dual capability to deliver daily, automated cell health and titer measurements from the same sample. This simultaneous analysis provides researchers with a comprehensive dataset encompassing both clone production and crucial indicators of cell viability and growth. Such an integrated approach offers a holistic view of cell culture performance, enabling well-informed decision-making throughout the development process.

The Cydem VT system leverages the fluorescence polarization detection method to achieve precise IgG quantification. By integrating this sophisticated detection method within the titer module and combining it with the trusted Vi-CELL BLU analyzer technology for cell health assessment, the Cydem VT system allows for the collection of high-quality and useful clone data.

Moreover, the automation of titer data collection within the Cydem VT system streamlines the entire workflow. By culturing clones and simultaneously measuring viability and titer production from the same sample, the system significantly reduces hands-on interaction. This automation minimizes the risk of human error, ensuring that valuable clones are not overlooked and suboptimal ones are not mistakenly selected. This also gives scientists more time to dedicate to other research, knowing that titer and cell health data will be collected automatically, promoting the efficiency of the laboratory.

The study demonstrated the Cydem VT system's repeatability of titer measurements and linearity across a wide range of IgG concentrations as evidenced by the strong correlation with the reference turbidimetric system, as well as robustness across different media types. Additionally, the 14-day fed-batch process confirmed that clone rankings obtained using the Cydem VT system were consistent with those from the offline reference device, further validating its applicability in CLD.

The Cydem VT system offers a robust, automated solution for IgG quantification, providing several advantages over traditional methods. Its ability to deliver reliable data through an automated, integrated workflow makes it a valuable tool to researchers. The Cydem VT system not only enhances the efficiency of titer measurements but also supports better informed decision-making in the clone-ranking process, leading to better quality of research.

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