Application of Maurice CE-SDS for Biopharmaceutical QC Workflows

Introduction

Protein identity, stability and purity are critical quality attributes of biopharmaceutical molecules that need to be closely monitored during the early phases of process development and late-phase batch lot release testing. Capillary electrophoresis (CE)-based methods can be efficiently applied for analytical quality control (QC) testing and provide a number of key advantages, including high separation efficiency, accurate quantitation, short analysis time, low waste generation and a diverse range of applications. As a result, CE methods are increasingly applied in the QC environment, replacing traditional slab gel and/or chromatography approaches.

Analysts performing CE may use an internal standard (IS) during batch runs for various reasons, including an effort to reduce sample injection variability, to correct for discrepancies in migration time and/or as a mobility marker. However, as an added external component, the IS also poses a risk for interfering with the separation of your test sample, which may result in uncertainties during data analysis and affect the reproducibility of results. Therefore, an alternative means for standardization is highly desirable.

In this application note, Maurice™ CE-SDS is evaluated on assay performance and method validation characteristics that are important for QC analytical testing using three reference molecules. We demonstrate the application of Maurice CE-SDS to a QC-specific workflow that eliminates the use of a commercial IS, thereby removing potential concerns such as introducing contaminants to test samples and interfering with subsequent analyses.

Introduction to Maurice CE-SDS

Maurice performs size-based CE-SDS on up to 48 samples per batch. The pre-assembled cartridge spares researchers the laborious capillary assembly, and maintenance and optimization steps required with other CE-based systems. There's no manual setup or maintenance required, and if there is a stoppage, he often just needs a cartridge replacement—not a disassembly for cleaning and maintenance. Maurice is a fully automated system with an easy-to-follow CE-SDS workflow: just pop in one of his cartridges, drop in your sample vials or a 96-well plate and hit start. Samples are electrokinetically injected into the cartridge capillary, based on their defined location in the batch, and subsequently electrophoresed within. The peaks are directly detected via UV absorbance at 220 nm and plotted on an electropherogram (e-gram). You can pre-program batch and method parameters, monitor your run in real-time and analyze data using Compass for iCE software that is compliant with the Food and Drug Administration (FDA) Title 21 Code of Federal Regulations Part 11 (21 CFR 11). Compass software has many tools to ensure data authenticity and integrity, including, but not limited to, restricted access, secure computer-generated time-stamped audit trails, e-signatures and compliant export or import function into third-party software like Chromeleon and Empower.

Materials and Methods

MAURICE CE-SDS APPLICATION KIT

The Maurice CE-SDS Application Kit (PN PS-MAK02-S) includes all batch reagents required for a run except β-mercaptoethanol (β-ME) and iodoacetamide (IAM). **Table 1** outlines the kit's components and the volumes added to each 2-mL glass reagent vial per batch. Note that each reagent must be capped with the appropriate orange or clear cap before placing them into the Maurice system for their correct loading into the capillary. Orange pressure caps denote injection by pressure and clear caps indicate injection by vacuum.

REAGENT	INDIVIDUAL PRODUCT NUMBER	VOLUME REQUIRED (ML)	CAP COLOR
Conditioning Solution 1	046-014	1.5	Orange
Conditioning Solution 2	046-015	1.5	Orange
Wash Solution	046-013	1.5 1.0	Clear Orange
Separation Matrix	046-386	1.5	Orange
Running Buffer	046-386	1.0	Clear
Deionized Water	—	1.5	Orange
Empty	—	—	Orange

TABLE 1. Maurice CE-SDS batch reagents and volume required per 2-mL glass reagent vial.

INFLIXIMAB

Infliximab is a monoclonal antibody against tumor necrosis factor-alpha. It has several approved uses, including treatment of rheumatoid arthritis, Crohn's disease, ulcerative colitis and psoriatic arthritis, as indicated by the FDA[1]. The infliximab sample used in this study was donated by a pharmaceutical collaborator. It was diluted in 1X Sample Buffer (PN 046-012) to the respective concentrations for further analysis, as described in the *Sample Preparation* and *Sample Running* sections.

NIST mAb

NIST mAb reference material (RM 8671, Lot 14HB-D-002) is a representative test molecule for the evaluation of therapeutic protein characterization technologies[2].

NIST mAb RM 8671 comes as an aqueous 10 mg/mL solution that was diluted in 1X Sample Buffer to the respective concentrations for further analysis, as described in the *Sample Preparation* and *Sample Running* sections.

MAURICE CE-SDS IgG STANDARD

The ProteinSimple IgG Standard (PN 046-039) was used as a system suitability sample. The IgG Standard comes lyophilized and was reconstituted in 50 µL of 1X Sample Buffer. It was diluted to the respective concentrations for further analysis, as described in the *Sample Preparation* and *Sample Running* sections.

SAMPLE PREPARATION

For all tests except linearity analyses, samples were diluted in 1X Sample Buffer to a final concentration of 1 mg/mL, from which 50-µL-aliquot samples were made. For linearity analyses, samples were first diluted in 1X Sample Buffer to a concentration of 1.5 mg/mL and further diluted to 0.75 mg/mL, 0.5 mg/mL and 0.25 mg/mL in a total volume of 50 µL per sample and injected in order of increasing concentration.

For the experiments addressing the alignment of e-grams (calibration), 2 µL of 25X CE-SDS IS (PN 046-144) previously reconstituted in 240 µL of 1X Sample Buffer was added only to those samples being used for comparison with alignment by way of the samples' antibody light chain.

For reduced conditions, 2.5 µL of a 14.2-M β-ME (Sigma-Aldrich, M6250) stock solution was added to each 50-µL sample. All samples were denatured at 70 °C for 10 minutes, cooled on ice for 5 minutes and mixed by vortex. For non-reduced conditions, 2.5 µl of a 250-mM stock solution of the alkylating agent IAM (Sigma-Aldrich, A3221) was added to each 50-µL sample to block disulfide scrambling or exchange. Each sample was then transferred to a 96-well plate and spun down in a centrifuge for 10 minutes at 1000 *x g*. For stressed conditions, samples were incubated at 37 °C for 72 hours prior to sample preparation.

SAMPLE RUNNING

All samples were electrokinetically injected into the cartridge capillary by applying 4600 V for 20 seconds before separation by electrophoresis at 5750 V. Reduced samples were separated for 25 minutes and non-reduced samples were separated for 35 minutes. Maurice conditions

the capillary, made of bare fused silica, at the beginning of a batch run with Conditioning Solution 1 (base), Conditioning Solution 2 (acid), deionized water and the Separation Matrix (**Table 1**). This process ensures the capillary surface is uniformly charged, so you get optimal resolution and assay reproducibility. Capillaries are then conditioned every 12 injections to maintain surface integrity. Bracketing injections of reference material were included before and after each capillary conditioning injection to confirm system suitability is maintained throughout the batch.

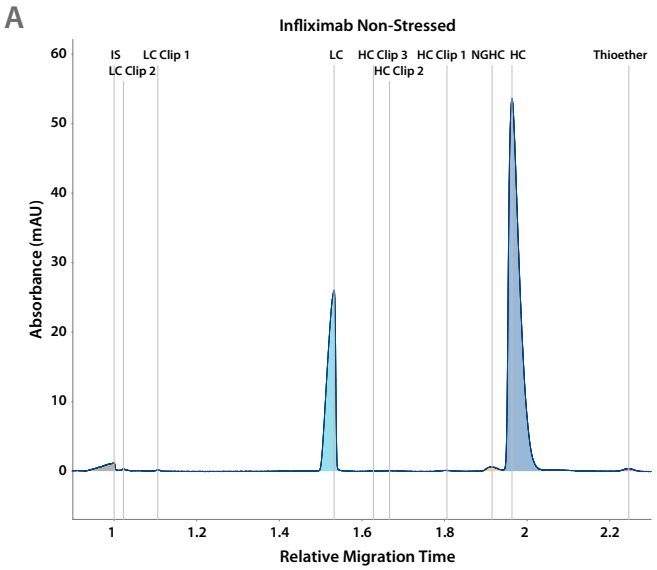
Qualification Testing and Results

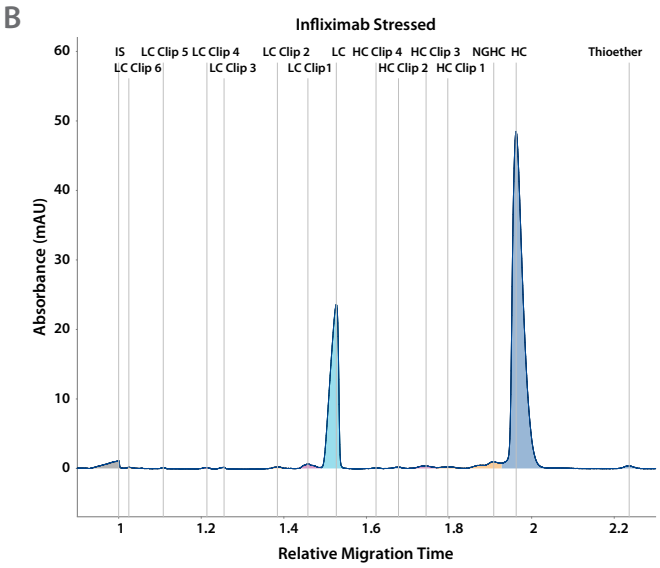
PRODUCT PEAK PROFILING

We first evaluated the selectivity and specificity of Maurice based on the ability to identify the various target profiles of the three antibodies tested, using demonstrated high-resolution of separation between the non-glycosylated heavy chain versus heavy chain (**Figure 1 and 2**). We then evaluated the selectivity and specificity of Maurice based on the ability to differentiate the target product peak from that of an IS peak (**Figure 3 and 4**), using either non-stressed or stressed samples and under non-reduced and reduced conditions. Non-reduced and reduced samples were analyzed in separate runs or allocated to opposite sides of a 96-well plate to prevent β-ME contamination, as the possibility for sample carry-over does not exist using the Maurice system.

As a practical example, we used infliximab. **Figure 1A and Figure 2A** show the typical separation obtained for the product under reduced and non-reduced conditions. As expected, compared with the non-reduced profile, the reduced target was only slightly affected by heat stress conditions (37 °C for 72 hours) (**Figure 1 A versus B**). Whereas with the non-reduced intact form, Maurice could specifically separate the resulting fragments (due to the same applied stress) from the main monomeric peak using the same separation conditions (**Figure 2 A versus B**), offering valuable information for product stability testing.

Similarly, under reduced conditions, the NIST mAb reference (**Figure 1 C versus D**) and ProteinSimple IgG Standard (**Figure 1 E versus F**) provide similar peak profiles and migration times for both non-stressed or stressed forms. Under non-reduced conditions, though, the temperature stress influenced the production of both high-molecular-weight and low-molecular-weight fragments, which Maurice efficiently separated and detected for both NIST mAb (**Figure 2 C versus D**) and the IgG Standard (**Figure 2 E versus F**).





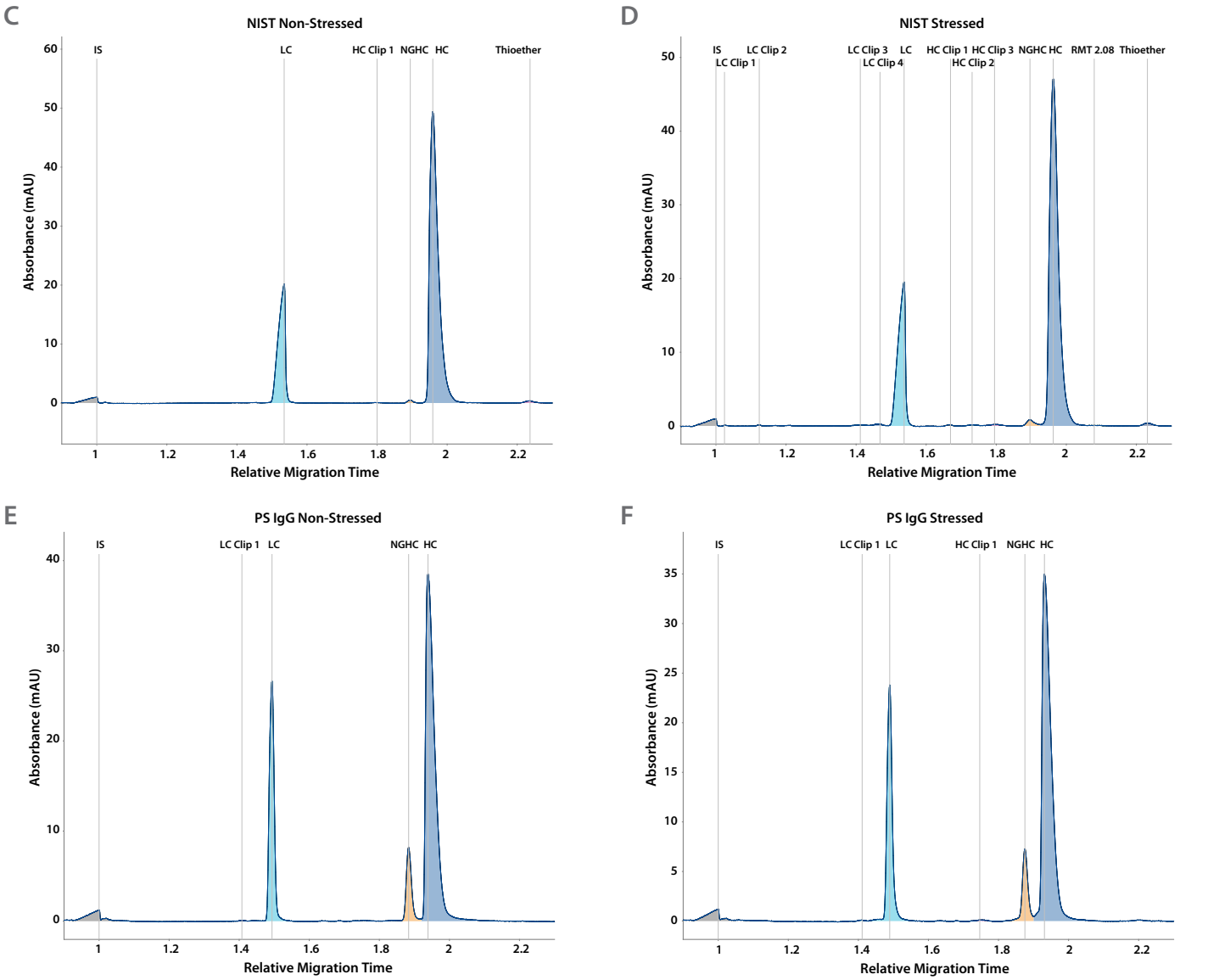
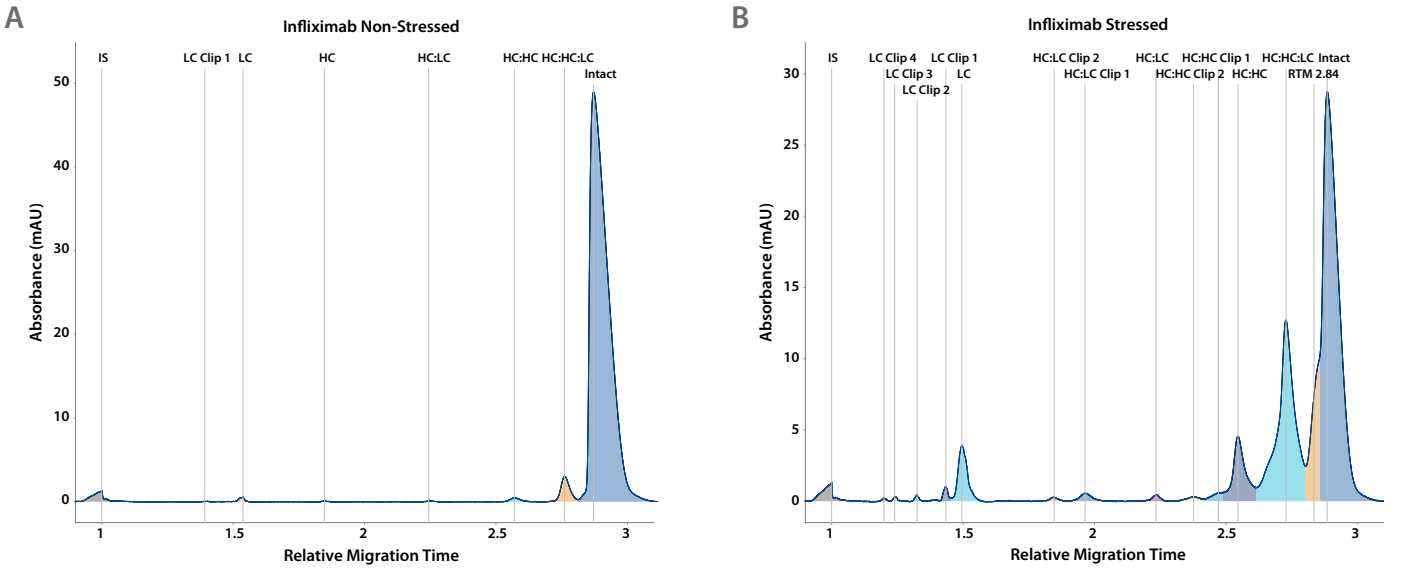


FIGURE 1. Target profiles under reduced conditions. Shown are side-by-side comparisons for non-stressed (left) and temperature stressed (right) samples of infliximab (A, B), NIST mAb (C, D) and the ProteinSimple IgG Standard (E, F). Each condition was run in triplicate and e-grams are representative of a series of three independent injections.



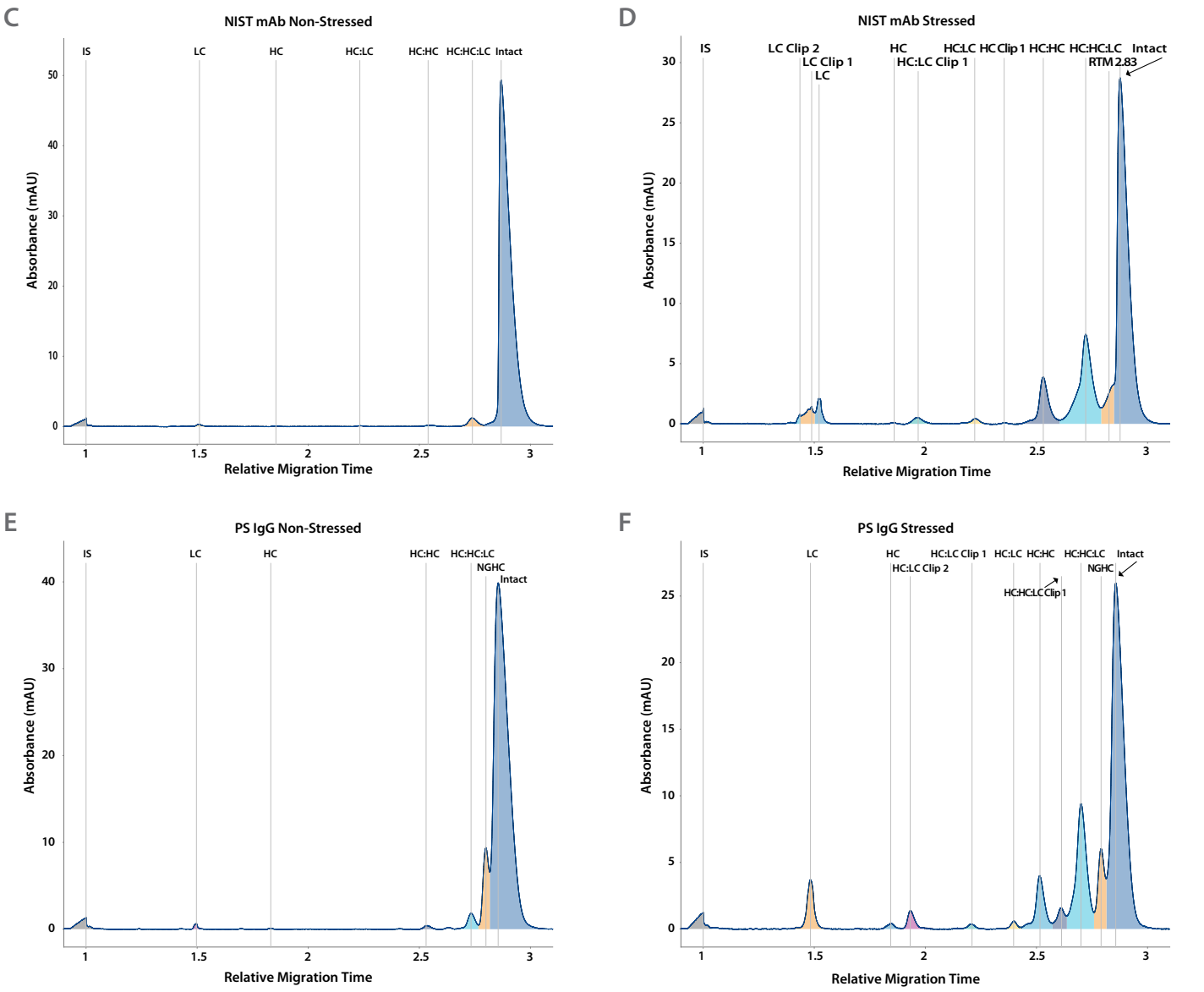


FIGURE 2. Target profiles under non-reduced conditions. Shown are side-by-side comparisons for non-stressed (left) and temperature stressed (right) samples of infliximab (A, B), NIST mAb (C, D) and the ProteinSimple IgG Standard (E, F). Each condition was run in triplicate and e-grams are representative of a series of three independent injections.

To demonstrate assay specificity, Maurice's ability to differentiate peaks generated by the product from those with an IS was assessed. **Figure 3 and Figure 4** compare non-stressed infliximab with the stressed sample under reduced and non-reduced conditions, respectively. By overlaying the e-gram of either reduced or non-reduced infliximab in the presence and absence of IS, we reveal that the product sample produces an early peak directly in line with that of added IS (**Figure 3 and 4**). Using stressed material (non-reduced or reduced), this is especially so (**Figure 3B and 4B**). Therefore, the inclusion of an IS for batch runs may not always be advantageous as it may mask a peak characteristic of stressed product samples.

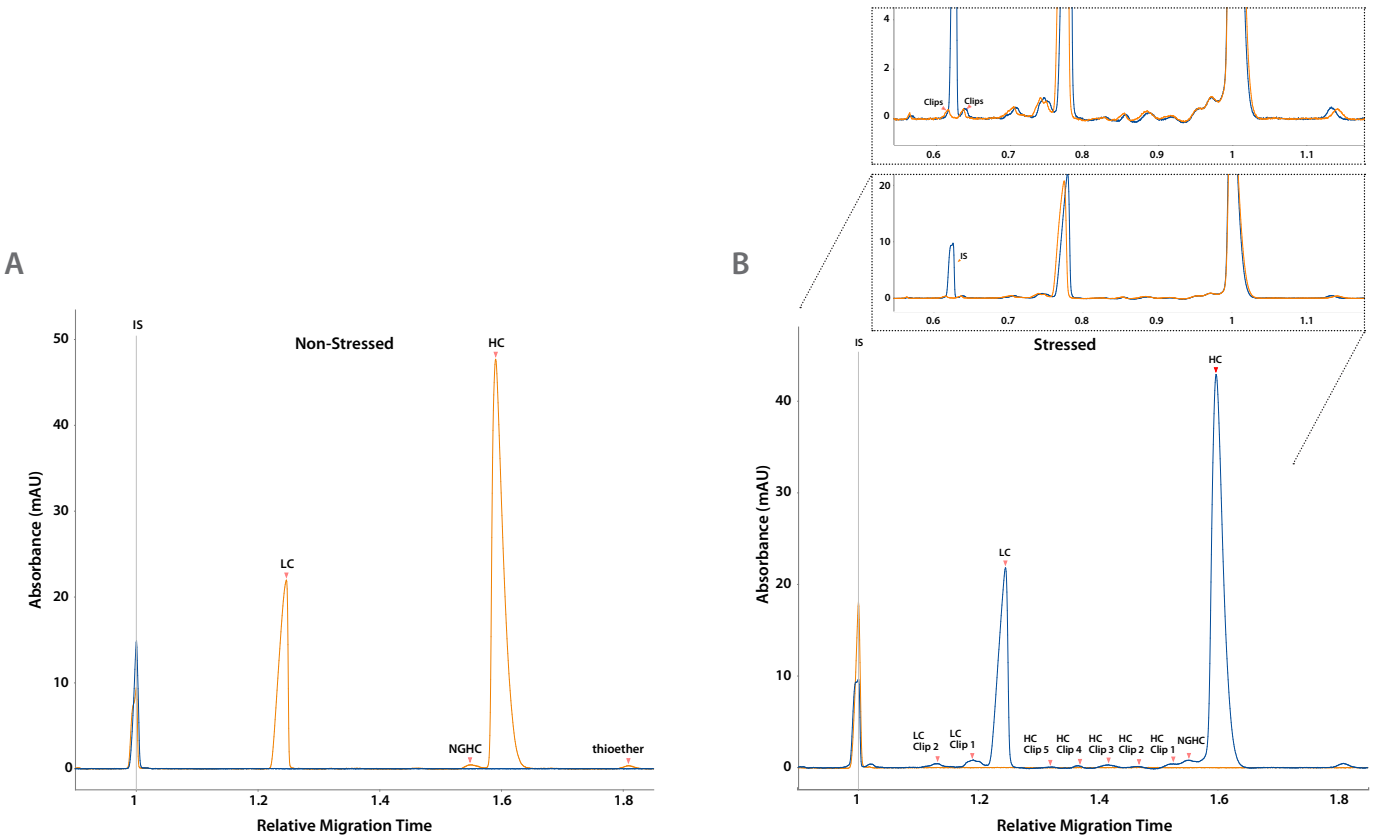


FIGURE 3. Target profile and IS e-gram overlays under reduced conditions. Shown are side-by-side comparisons for non-stressed (A) and temperature stressed (B) samples of infliximab, including a higher magnification of the e-gram for visual clarity. Blue trace: IS only; Orange trace: Infliximab mixed with IS

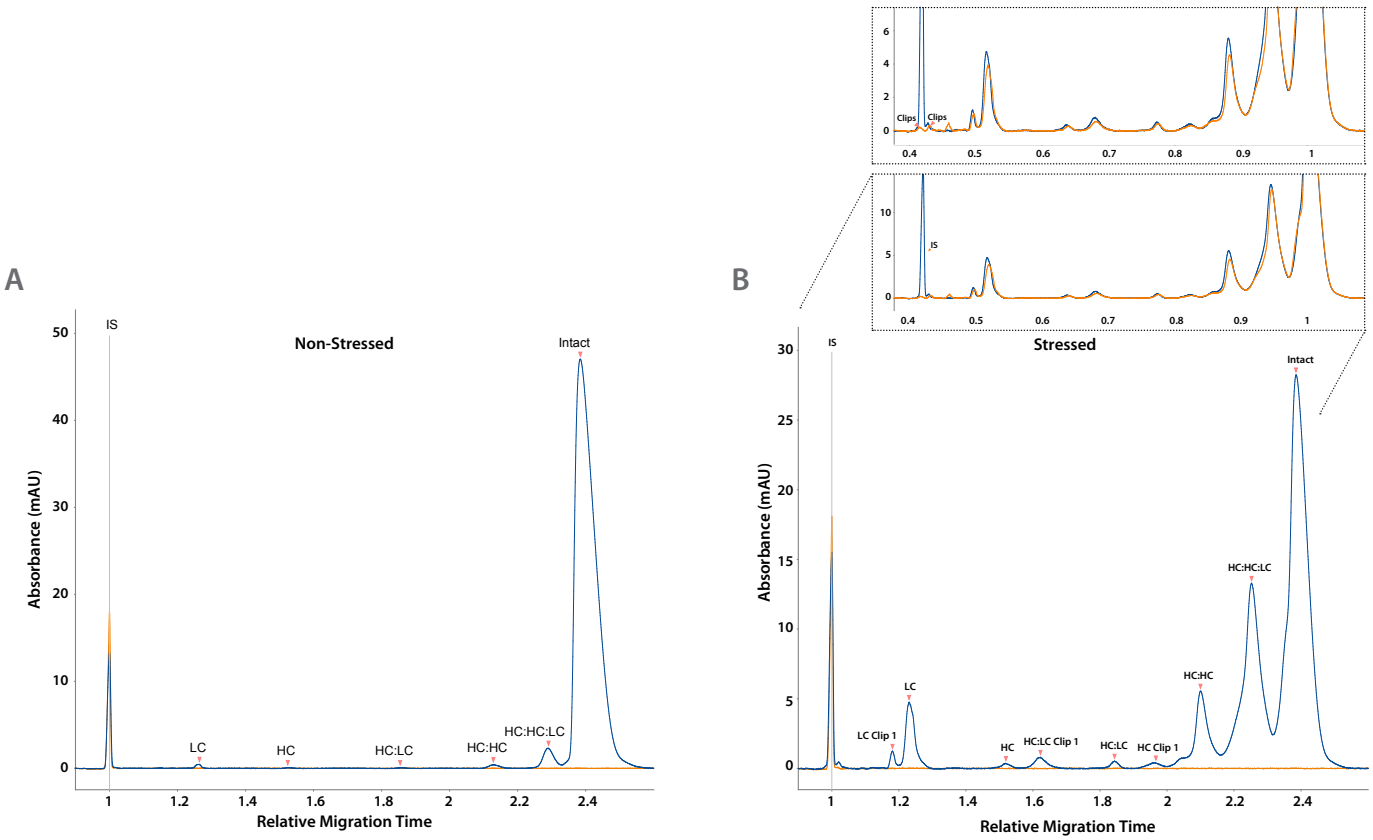


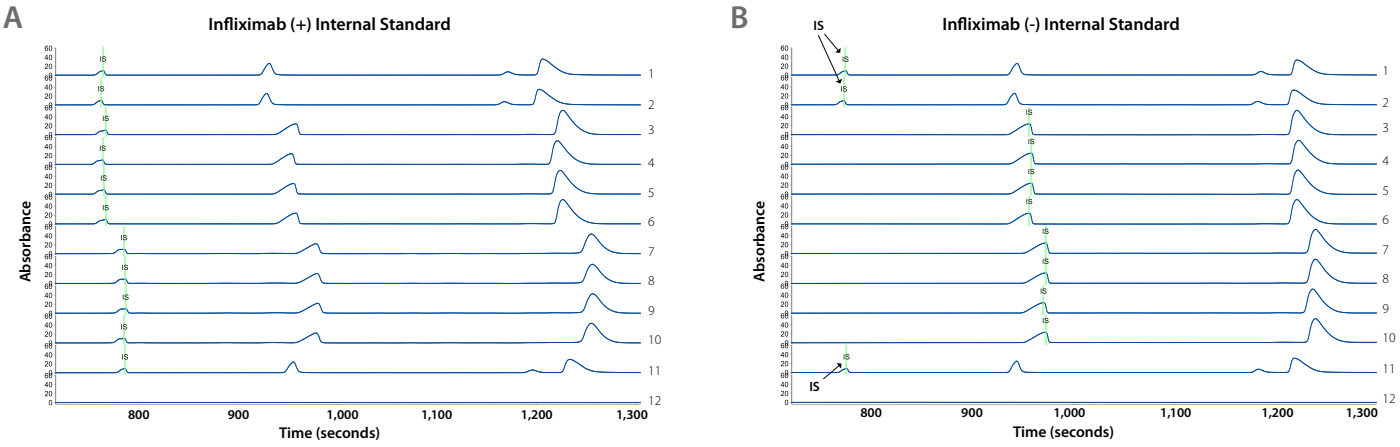
FIGURE 4. Target profile and IS e-gram overlays under non-reduced conditions. Shown are side-by-side comparisons for non-stressed (A) and temperature stressed (B) samples of infliximab, including a higher magnification of the e-gram for visual clarity. Orange trace: IS only; Blue trace: Infliximab mixed with IS

CALIBRATION: NO INTERNAL STANDARD REQUIRED

A QC-specific workflow that removes the need for a commercial IS has two primary advantages: no need to supplement the sample with added components and, therefore, no interference with analysis. Instead, the antibody sample's light chain can be used for calibration as it is present in both reduced and non-reduced sample types, albeit in low levels in the latter. In some cases, during QC testing of samples, the purified light chain from the reference sample could be spiked into the blank for alignment. This spiking was not performed in these experiments.

In the next set of experiments, we compare reduced and non-reduced Maurice CE-SDS sample batch data using infliximab, NIST mAb and our in-house IgG Standard with and without the inclusion of a commercially available IS. Again, ProteinSimple recommends allocating sample wells for non-reduced samples to one side of a 96-well plate and reduced samples to the other to prevent sample mix-up and β-ME cross-contamination. **Figures 5 and 6** illustrate example comparative e-grams for reduced and non-reduced infliximab and ProteinSimple IgG Standard, respectively. Twelve total injections are shown, of which four are dedicated to non-stressed samples and another four to temperature stressed samples for both reduced (**Figure 5**) and non-reduced conditions (**Figure 6**). The eight injections containing target were bracketed with a reference sample, and a blank injection (Sample Buffer) was included for each batch run.

Based on the results obtained, Maurice can perform calibration using the sample's light chain without adversely affecting assay resolution, reproducibility or migration time, summarized in **Tables 2, 3, 4 and 5**. For reduced samples, the quantitation of peak area percent for heavy chain plus light chain was within ±5% of each other across non-stressed and temperature-stressed samples, regardless of the presence of an IS, with overall relative standard deviation (RSD) values less than 1% (**Table 2**). For non-reduced samples, the influence of temperature stress had a globally larger effect on the average peak area percent calculated for each intact mAb sample (**Table 3**). However, similar reproducibility is achieved, noted by peak area RSD values once again far below 1% for non-stressed and stressed sample types. To further attest to the feasibility of using the light chain for alignment without negatively impacting CE-SDS results, in **Table 4 and Table 5** we summarize the measured relative migration time and include RSD calculations, for reduced and non-reduced conditions, respectively. Migration time reflects not only the distance traveled but also the migration velocity, an attribute specific to the system that is dependent on the capillary length and the applied voltage[3]. Overall, the three antibody samples, infliximab, NIST mAb and the ProteinSimple IgG Standard displayed average migration times that were unaffected by stress conditions or the presence/absence of an IS. For reduced conditions, the average migration times were all within a 30-second difference of each sample analyzed, and RSD was ≤0.7% (**Table 4**). The migration time for non-reduced samples was expectedly longer than that of reduced samples, but, again, within only a 30-second difference between the three antibodies, infliximab, NIST mAb or ProteinSimple IgG Standard, under stressed or non-stressed conditions (**Table 5**). RSD values were also ≤0.7% for non-reduced samples.



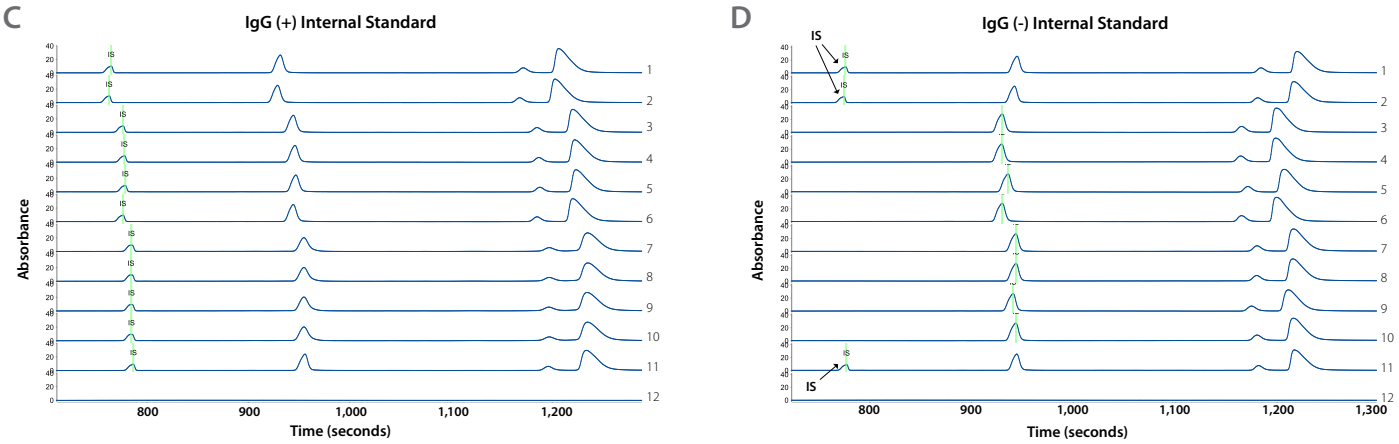


FIGURE 5. Light chain calibration under reduced conditions. Shown are side-by-side comparative e-grams, each including 12 injections, with and without IS, for infliximab (A, B) and the ProteinSimple IgG standard (C, D). The left panel includes the addition of a commercial IS to all samples analyzed (injections 1–11). The right panel uses the sample's light chain for all injections, except 1, 2 and 11 where the IS was added for comparison in the same batch run. Samples injected are as follows: Injection 1 = conditioning (system suitability reference); injections 2 and 11 = reference bracket; injection 3–6 = non-stressed and reduced sample; injection 7–10 = stressed and reduced sample; injection 12 = blank (sample buffer).

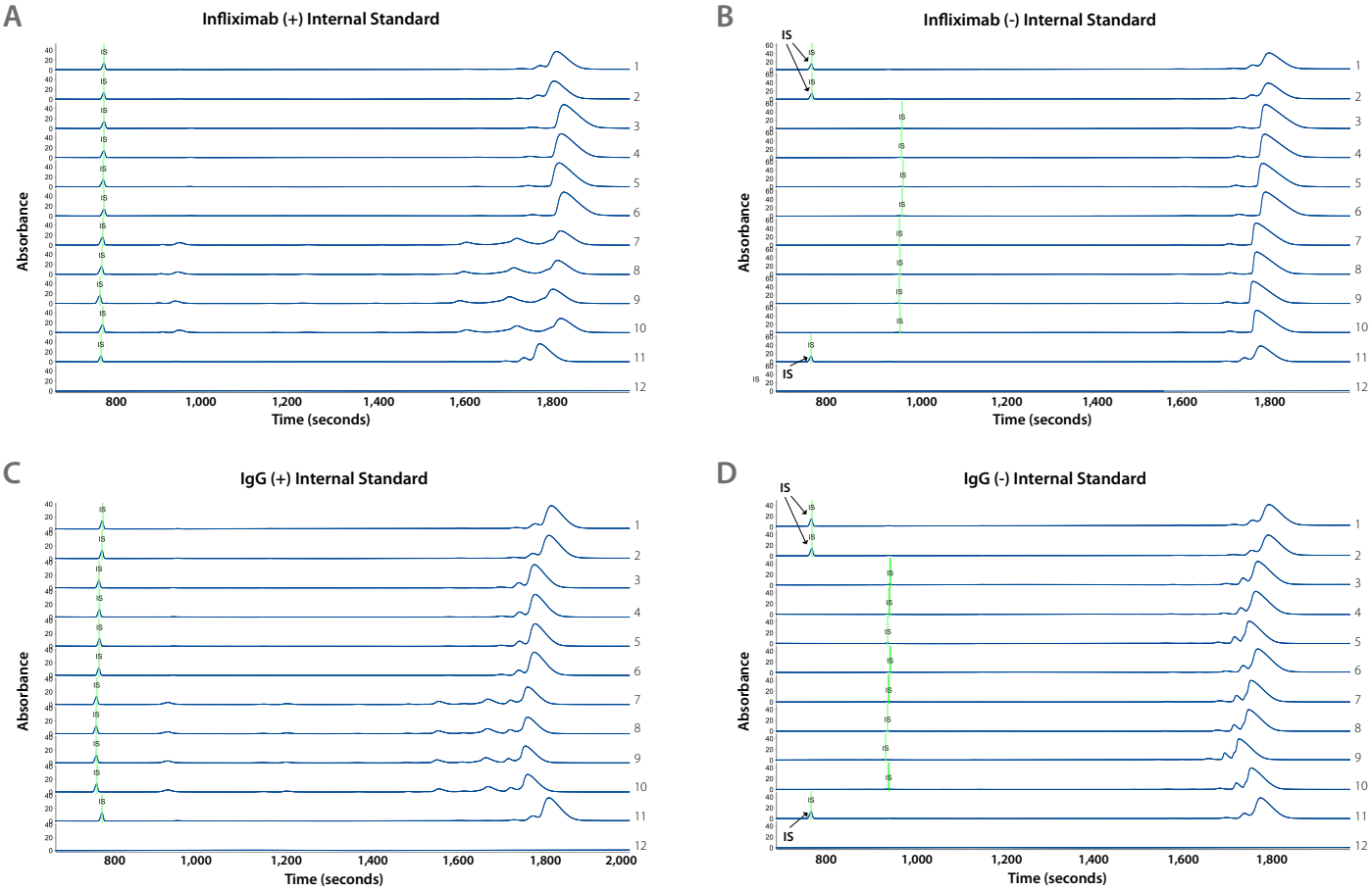


FIGURE 6. Light chain calibration under non-reduced conditions. Shown are side-by-side comparative e-grams, each including 12 injections, with and without IS, for infliximab (A, B) and the ProteinSimple IgG Standard (C, D). The left panel includes the addition of a commercial IS to all samples analyzed (injections 1–11). The right panel uses the sample's light chain for all injections, except 1, 2 and 11 where the IS was added for comparison in the same batch run. Samples injected are as follows: Injection 1 = conditioning (system suitability reference); injections 2 and 11 = reference bracket; injection 3–6 = non-stressed and non-reduced sample; injection 7–10 = stressed and non-reduced sample; injection 12 = blank (sample buffer).

		NON-STRESSED		STRESSED	
		(+) Internal Standard	(-) Internal Standard	(+) Internal Standard	(-) Internal Standard
Infliximab	Average (%)	98.8	98.1	95.7	93.8
	Std. Dev	0.00	0.30	1.40	0.30
	% RSD	0.00	0.30	1.50	0.30
NIST mAb	Average (%)	99.1	99.0	96.6	96.8
	Std. Dev	0.10	0.10	0.10	0.30
	% RSD	0.10	0.10	0.10	0.30
IgG Standard	Average (%)	92.3	92.0	91.4	91.1
	Std. Dev	0.40	0.40	0.40	0.50
	% RSD	0.40	0.40	0.40	0.60

TABLE 2. Percent peak area analysis for reduced conditions (heavy chain plus light chain).

		NON-STRESSED		STRESSED	
		(+) Internal Standard	(-) Internal Standard	(+) Internal Standard	(-) Internal Standard
Infliximab	Average (%)	95.9	95.5	53.2	48.0
	Std. Dev	0.30	0.00	0.10	0.30
	% RSD	0.40	0.10	0.20	0.70
NIST mAb	Average (%)	96.7	96.8	58.5	56.1
	Std. Dev	0.20	0.20	0.10	0.10
	% RSD	0.30	0.20	0.20	0.20
IgG Standard	Average (%)	87.5	87.9	55.1	53.2
	Std. Dev	0.60	0.10	0.10	0.10
	% RSD	0.70	0.10	0.20	0.30

TABLE 3. Percent peak area analysis for non-reduced conditions (intact protein).

		NON-STRESSED		STRESSED	
		(+) Internal Standard	(-) Internal Standard	(+) Internal Standard	(-) Internal Standard
Infliximab	Average (%)	1090.0	1091.6	1117.7	1090.4
	Std. Dev	4.90	3.40	1.60	3.00
	% RSD	0.40	0.30	0.10	0.30
NIST mAb	Average (%)	1100.1	1103.3	1121.6	1107.4
	Std. Dev	7.30	3.50	0.40	4.50
	% RSD	0.70	0.30	0.00	0.40
IgG Standard	Average (%)	1083.9	1058.1	1094.9	1062.6
	Std. Dev	2.90	2.40	0.50	3.30
	% RSD	0.30	0.20	0.00	0.30

TABLE 4. Average migration time for reduction conditions.

		NON-STRESSED		STRESSED	
		(+) Internal Standard	(-) Internal Standard	(+) Internal Standard	(-) Internal Standard
Infliximab	Average (%)	1831.2	1806.0	1821.1	1818.9
	Std. Dev	5.50	5.70	8.80	3.80
	% RSD	0.30	0.30	0.50	0.20
NIST mAb	Average (%)	1838.4	1845.8	1815.0	1849.3
	Std. Dev	2.40	2.60	1.10	4.00
	% RSD	0.10	0.10	0.10	0.20
IgG Standard	Average (%)	1781.4	1787.5	1762.3	1785.4
	Std. Dev	1.00	4.60	3.10	2.30
	% RSD	0.10	0.30	0.20	0.10

TABLE 5. Average migration time for non-reduced conditions.

A NEW LEVEL OF LINEARITY

The linearity of assay detection was examined as a measure of concentration versus area for all three antibodies as either stressed or non-stressed material under reduced or non-reduced conditions. **Table 6 and Table 7** summarize the linearity of detection under reduced and non-reduced conditions, respectively, using the peak area versus protein concentration measured from the injection of increasing concentrations (0.25, 0.50, 0.75, 1.00, 1.50 mg/mL) of either infliximab, NIST mAb or ProteinSimple IgG Standard, run in triplicates. For this concentration range, a very strong coefficient of determination (R^2) was achieved for non-stressed (≥0.99) and stressed (≥0.97) infliximab, NIST mAb and IgG samples under reduced conditions (**Table 6**). Similarly, for non-reduced conditions, R^2 values ≥0.99 were determined for non-stressed samples and ≥0.96 for stressed infliximab, NIST mAb or ProteinSimple IgG Standard (**Table 7)**. Taken together, these data demonstrate Maurice's ability to assess product purity accurately.

	NON-STRESSED (R^2)	STRESSED (R^2)
Infliximab	0.9966	0.9948
NIST mAb	0.9979	0.9891
IgG Standard	0.9909	0.9767

TABLE 6. Assay linearity as a measure of peak area versus concentration for reduced conditions.

	NON-STRESSED (R^2)	STRESSED (R^2)
Infliximab	0.9938	0.9740
NIST mAb	0.9969	0.9624
IgG Standard	0.9936	0.9647

TABLE 7. Assay linearity as a measure of peak area versus concentration for non-reduced conditions.

PROLONGED PRECISION

Experimental precision was first measured in terms of experimental repeatability using triplicate 1-mg/mL injections of NIST mAb, ProteinSimple IgG Standard and infliximab sample, daily, over a three-day period. Results were collected, analyzed and are presented for each day. On the third day, the Maurice CE-SDS cartridge was changed and had no impact on the results obtained. Experimental setup included automatic conditioning at the start of each 12-injection increment and reference bracketing of our samples for injection.

To assess Maurice's ability to reliably repeat results in the event a degraded product is encountered, we subjected all three antibodies to accelerated degradation at 37 °C for an incubation period of 72 hours prior to analysis. This was performed for both reduced and non-reduced sample types. **Table 8** summarizes the results of the reduced assay, where the RSD of percent area of the heavy and light chain peaks was <0.5% for all non-degraded samples run and ≤1.5% for the degraded samples over the three-day period. For non-reduced assay conditions, the calculation of percent peak area for the intact protein peak produced RSD values that were consistently ≤1% (**Table 9**). Intermediate precision, or within-lab reproducibility as it's sometimes called, is also reported, using identical experimental conditions as for repeatability, but averaging the three-day datasets for a total of nine injections analyzed (**Table 10 and Table 11**). From the nine replicate analyses, the RSD values calculated are slightly higher than those for the repeatability injection series of runs, but still below 2% for both non-degraded and degraded infliximab, NIST mAb and ProteinSimple IgG Standard under reduced (**Table 10**) or non-reduced (**Table 11**) conditions. Overall, the three-day average percent peak area RSD values showed that Maurice could reliably reproduce results over time, even if conditions change or the sample is degraded and, therefore, of poor quality.

		NON-DEGRADED			DEGRADED (ACCELERATED)		
		Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
Infliximab	Average	98.8	99.1	98.9	95.7	97.9	98.0
	Std. Dev	0.0	0.4	0.2	1.4	1.1	0.6
	% RSD	0.0	0.4	0.2	1.5	1.1	0.7
NIST mAb	Average	99.1	99.1	99.2	96.6	98.0	98.1
	Std. Dev	0.1	0.0	0.2	0.1	0.8	0.8
	% RSD	0.1	0.0	0.2	0.1	0.8	0.8
IgG Standard	Average (%)	92.3	92.4	92.5	91.4	91.9	91.4
	Std. Dev	0.4	0.1	0.1	0.4	0.4	0.3
	% RSD	0.4	0.1	0.1	0.4	0.4	0.4

TABLE 8. Assay repeatability using the sum of the percent peak area of the heavy chain plus that of the light chain under reduced conditions..

		NON-DEGRADED			DEGRADED (ACCELERATED)		
		Day 1	Day 2	Day 3	Day 1	Day 2	Day 3
Infliximab	Average)	95.9	93.3	92.1	53.2	52.9	52.9
	Std. Dev	0.3	0.2	0.3	0.1	0.5	0.1
	% RSD	0.4	0.2	0.4	0.2	1.0	0.2
NIST mAb	Average	96.7	93.0	93.4	58.5	58.6	58.6
	Std. Dev	0.2	0.5	0.7	0.1	0.2	0.1
	% RSD	0.3	0.6	0.7	0.2	0.3	0.2
IgG Standard	Average	87.5	88.5	86.0	55.1	54.8	56.3
	Std. Dev	0.6	0.3	0.3	0.1	0.3	0.5
	% RSD	0.7	0.3	0.4	0.2	0.5	1.0

TABLE 9. Assay repeatability using the sum of the percent peak area of the intact protein peak under non-reduced conditions.

		NON-DEGRADED	DEGRADED (ACCELERATED)
Infliximab	Average)	98.9	97.2
	Std. Dev	0.4	1.7
	% RSD	0.4	1.7
NIST mAb	Average	99.1	97.6
	Std. Dev	0.5	1.1
	% RSD	0.5	1.1
IgG Standard	Average	92.4	91.6
	Std. Dev	0.5	0.9
	% RSD	0.6	0.9

TABLE 10. Intermediate precision, reduced assay.

		NON-DEGRADED	DEGRADED (ACCELERATED)
Infliximab	Average)	93.7	53.0
	Std. Dev	1.7	0.3
	% RSD	1.8	0.6
NIST mAb	Average	94.3	58.6
	Std. Dev	1.8	0.1
	% RSD	1.9	0.2
IgG Standard	Average	87.3	55.5
	Std. Dev	1.1	0.9
	% RSD	1.3	1.6

TABLE 11. Intermediate precision, non-reduced assay.

Conclusions

In this study, we outline the development of a quality-controlled assay that includes specifications for the evaluation of product purity and stability in both a reduced or non-reduced protein state. We've shown you that using the antibody's light chain for calibration does not affect the quality of data you'll generate with Maurice, thereby eliminating the addition of a commercial IS to each sample. To demonstrate the suitability of each assay, we include an IgG control and the NIST mAb reference material for comparison with infliximab, a practical product sample.

The CE-SDS workflow using Maurice provides for rapid analysis and platform methods, which make Maurice a valuable system for biopharmaceutical QC testing. His simplified workflow removes multiple manual steps that need to be meticulously performed and maintained, when using conventional CE-SDS systems, which certainly reduces the chance of analyst error. And, once your samples and reagents are prepared, it takes less than 10 minutes to start a batch. With Maurice CE-SDS, you can perform in-process and batch lot release QC analyses of a biotherapeutic agent using a much simpler workflow, resulting in higher quality data than you may currently be collecting.

References

1. Infliximab, R Fatima and M Aziz, *StatPearls*, Available online at https://www.ncbi.nlm.nih.gov/books/NBK500021/. Accessed July 2, 2018. Updated April 24, 2018.

2. National Institute of Standards and Technology, NIST Monoclonal Antibody Reference Material 8671. Available online at https://www.nist.gov/programs-projects/nist-monoclonal-antibody-reference-material-8671. Accessed July 2, 2018. Updated February 9, 2018.

3. A Ahuja and M Jimidar, editors, *Capillary Electrophoresis Methods for Pharmaceutical Analysis* Volume 9. Academic Press, 2008.

proteinsimple a bio-techne brand

Toll-free: (888) 607-9692
Tel: (408) 510-5500
info@proteinsimple.com
proteinsimple.com