

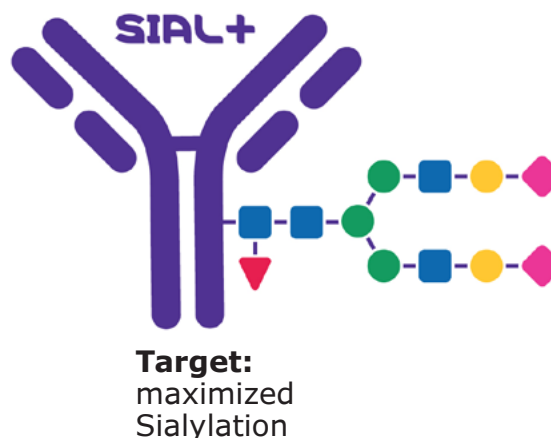
Cellvento® ModiFeed Sial+ COMP

Chemically defined Cell Culture Feed designed to maximize Sialylation

Product Description

Cellvento® ModiFeed Sial+ is a chemically defined feed formulation containing only components of non-animal origin. The product is intended for use in the development and further manufacturing of monoclonal antibodies (mAbs) and next-generation biopharmaceuticals in Chinese hamster ovary (CHO) cell-based expression systems. For ease of use, the product is supplied as a compacted dry powder – a convenient to handle and hydration-friendly format.

Cellvento® ModiFeed Sial+ is a **complete feed**. It is **highly concentrated**, one-part, pH neutral, and designed to be added to replenish depleted nutrients required for cellular function and to extend the production phase in fed-batch, while simultaneously **maximizing sialylation** on the protein of interest.



Application

Glycosylation is known to have effects on the biological activity, solubility, serum half-life, and safety of therapeutic proteins. In a fed-batch process, cells are initially grown in a lean production medium followed by routine feeding to achieve the desired product yield. Control of protein glycosylation, such as sialylation, while maximizing productivity is key for successful therapeutic protein development and production. For example, N-glycosylations of IgG Fc, particularly sialylation, has been reported to exert significant anti-inflammatory effects. Changes in the level of sialylation are also factors that shape the development of certain autoimmune diseases. As a result, high sialylation levels can help to increase stability, safety, and efficacy of the protein of interest. At the same time, full control of the sialylation levels is critical.

Cellvento® ModiFeed Sial+ Feed was developed to increase sialylation while maintaining or improving product titer. Besides maximizing sialylation level, the sialylation profile can be tailored as needed when combining Cellvento® ModiFeed Sial+ Feed with Cellvento® ModiFeed Prime Feed and administering the combination as a single feed (see section B. *Initial sialylation level optimizing evaluation* for more details).

This product is intended for research or further manufacturing but not for human or therapeutic use.

Benefits of Cellvento® ModiFeed Sial+ include:

- Complete feed maximizing sialylation.
- Chemically defined, non-animal origin – providing increased process control and less complexity.
- Compacted feed – reducing the complexity of hydration, storage, and feeding.
- Hydrated feed is stable at room temperature – no temperature cycling required during processing.
- Highly concentrated – allowing for a reduced volume of feed, thereby increasing product yield.
- No hydrolysates, phenol red, or 2-mercaptoethanol – ensuring batch-to-batch consistency.
- No glucose – enabling greater control of glucose concentration during a fed-batch process.

Storage

Store product in original packaging at 2 – 8 °C protected from light.

Do not use after expiration date. Avoid opening and closing container multiple times.

Shelf life is provided with the CoA or shelf-life information sheet.

Reconstitution method – Cellvento® ModiFeed Sial+ Feed

1. Slowly add 155.8 g/L of compacted powder to 85% of final volume Milli-Q® or similar cell culture grade water (18 – 25 °C) in an appropriately sized container.
2. Rinse weighing vessel as necessary to remove remaining compacted powder.
3. Vigorously mix for at least 10 minutes, solution will still be slightly turbid.
4. Using a calibrated vessel adjust to 100% volume (QS) with Milli-Q® or similar cell culture grade water (18 – 25 °C).
5. Vigorously mix for at least 90 minutes until solution is clear.
6. Measure final pH: Expected pH 6.8 ± 0.3 .
7. Measure final osmolality: Expected osmolality $1,400 \pm 75$ mOsm/kg.
8. Immediately filter using a sterilizing-grade filter ($\leq 0.22 \mu\text{m}$). Filter recommendations are provided below.
9. Store reconstituted Cellvento® ModiFeed Sial+ Feed protected from light at 2-8 °C for up to 90 days or at room temperature (18 – 25 °C) for up to 30 days.

NOTE: This feed does NOT contain glucose.

Recommended feeding strategy

Cellvento® ModiFeed Sial+ has been developed to be used as a feed in combination with either the production media Cellvento® 4CHO or EX-CELL® Advanced CHO but the use is not limited to these combinations. As with most upstream bioprocesses, optimization of feed volumes and timing of feed administration should be empirically determined on a process and cell line specific basis to maximize performance.

Cellvento® ModiFeed Sial+ Feed, used in conjunction with Cellvento® 4CHO or EX-CELL® Advanced CHO media, is recommended to be fed at between 17.5% and 22.5% total feed, depending on the demands of the clone(s) tested.

A. Initial feeding evaluation

The use of Cellvento® ModiFeed Sial+ as sole feed to maximize sialylation level of a biotherapeutic protein is described in the instruction below (see section A. *Suggested initial feeding evaluation*).

B. Adjustment option

To obtain a desired sialic acid content on the protein of interest, Cellvento® ModiFeed Sial+ can be used as part of a mixed feed to target a specific glycosylation profile in combination with Cellvento® ModiFeed Prime (see section B. *Evaluation and Optimization of the sialylation level* for more detail).

Parameter	Recommended range for evaluation
Cellvento® ModiFeed Sial+ COMP	2.5% – 7.5% (v/v) per feed
Frequency	48 – 72 hours feed interval
Glucose	4 – 8 g/L monitor, maintain and adjust accordingly

A. Suggested initial feeding evaluation

To identify the optimum approach for the clone(s) being tested, initial evaluation should consist of 17.5% and 22.5% total feed. A low percentage has the potential to underfeed while a high percentage has the potential to overfeed. Unless the general demands of the clone(s) are already known, during initial evaluation it is suggested to test both a low and high total feed percentage.

Important considerations:

- Initiate the feeding only when viable cell density is $\geq 2 \times 10^6$ cells/mL and no earlier than day three (to avoid over-feeding).
- Maintain supplementation with feed supplements and glucose until culture viability is less than 80%.
- Terminate and harvest cultures when viability drops below 70%.

Culture Day	Total Feed	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total Feed (%)
Cellvento® ModiFeed Sial+ COMP (% v/v)	Low				3		3		5.5			3		3			17.5
Cellvento® ModiFeed Sial+ COMP (% v/v)	High				4		4		6.5			4		4			22.5

If preferred, the schedule can be adjusted to support a more regular feed interval:

Culture Day	Total Feed	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total Feed (%)
Cellvento® ModiFeed Sial+ COMP (% v/v)	Low				3.5		3.5		3.5		3.5		3.5				17.5
Cellvento® ModiFeed Sial+ COMP (% v/v)	High				4.5		4.5		4.5		4.5		4.5				22.5

Once a preference for a lower or higher total feed percentage is established, optimization through further increasing or decreasing the total feed can be evaluated.

The suggested initial feeding evaluation is designed to support a low seed ($2 - 5 \times 10^5$ cells/mL) 14 day fed-batch process. If viability is still high late in culture, longer fed-batches can be supported. Additional feeding may be required. Continue with similar feeding frequency and percentages until viability drops below 80%.

A high seed fed-batch ($2 - 10 \times 10^6$ cells/mL) may require adjustment in feeding schedule to support higher biomass earlier in culture and provide more total feed. Feeding can be initiated as early as day 2 to support higher biomass early in culture. High seed may offer an option for shortening the duration of longer fed-batches or for achieving increased production over the same 14 days.

B. Evaluation and Optimization of the sialylation level

Cellvento® ModiFeed Sial+ Feed should be used at 100% to maximize sialylation on terminal glycans of therapeutic proteins.

If targeting a specific sialylation profile is required, the feeds Cellvento® ModiFeed Sial+ and Cellvento® ModiFeed Prime can be mixed. This method will increase terminal sialic acid to a desired target level because the concentration of sialylation-increasing modulators is decreased and thus users can target a specific sialylation profile. Testing will be required to optimize the ratio of these two feeds. The same feed regiment should be employed as described in section A. *Suggested initial feeding evaluation.*

Prepare both feeds per each product's hydration instructions. After sterile filtration, the two complete feeds can be mixed in a sterile container and should be protected from light. The created feed is complete and can be administered throughout a fed-batch as a single feed.

Initial testing mix suggestion for Cellvento® ModiFeed Prime and Cellvento® ModiFeed Sial+ Feed is shown in the example below:

(%) Cellvento® ModiFeed Prime Feed	(%) Cellvento® ModiFeed Sial+ Feed
0	100
50	50
75	25
87.5	12.5
93.75	6.25
96.87	3.13
98.44	1.56
99.22	0.78
100	0

When Cellvento® ModiFeed Prime Feed is mixed with Cellvento® ModiFeed Sial+ Feed, a titration of the impact on sialylation is observed (**see Figure**). Feasible range is affected by the basal media, in combination with either Cellvento® ModiFeed Sial+ Feed (highest point) or Cellvento® ModiFeed Prime Feed (lowest point).

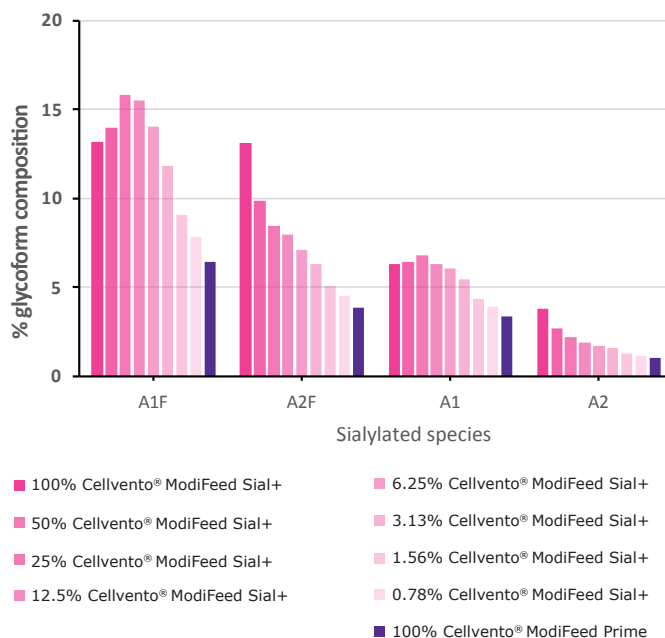


Figure: Glycosylation profile of CHO clone in Cellvento® 4CHO on day 12 with a varying composition of fed-batch culture feed.

Ordering Information

Cat. No.	Description	Application	Pkg. Size	Equivalent (L)
1.04662.0001	Cellvento® ModiFeed Sial+ COMP	High Sialylation Feed	155.8 g	1
1.04662.0005	Cellvento® ModiFeed Sial+ COMP	High Sialylation Feed	0.779 kg	5
1.04662.0050	Cellvento® ModiFeed Sial+ COMP	High Sialylation Feed	7.790 kg	50

Related Products

Cat. No.	Description	Application	Pkg. Size	Equivalent (L)
1.03795	Cellvento® 4CHO COMP	Fed-batch medium	Multiple	1, 10, 100
24366C	EX-CELL® Advanced CHO	Fed-batch medium	Multiple	1, 10, 100
14366C	EX-CELL® Advanced CHO	Fed-batch medium	1000 mL	1
1.04132	Cellvento® ModiFeed Prime COMP	Fed-batch feed	Multiple	1, 5, 50

Filters

The following sterilizing-grade filters are recommended for use with Cellvento® ModiFeed Sial+ Feed:

Organism Removal	Bacteria Removal	Mycoplasma & Bacteria Removal
Volume (L)	Millipore Express® SHC	Millipore Express® SHR with Prefilter
5 – 50	KHGES015FF3	KHVES015FF3
500	KHGES03TT3	KHVES05TT1

Cellvento® ModiFeed Sial+ Feed is supported by the Emprove® Program – The Smart Way to Master Compliance and Control.

Complementing our product portfolio, the Emprove® Program provides convenient access to reliable technical, regulatory, and supply information in Emprove® Dossiers to support your risk assessment continuum. A subscription to our Emprove® Suite can help you stay current: In addition to accessing the Emprove® Dossiers, you can also receive notification updates to document changes, as well as generate metrics and reports.

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