



## A case study: Cytokine cost calculation for a T cell transduction run

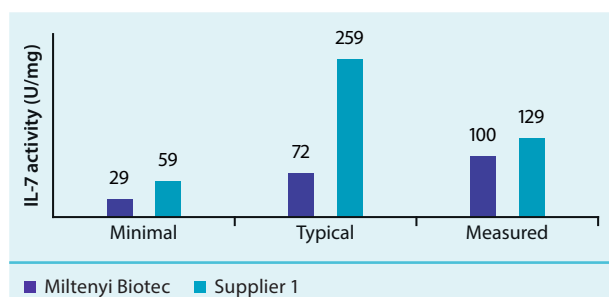
Clinical-grade cytokines and other ancillary materials make up a substantial part of the costs of cellular products. It is common practice to calculate these costs based on minimal or typical activity values given by the supplier, since this determines how much of the cytokine is needed for the application. In practice, activity values can deviate from this stated performance, making the estimations inaccurate.

As an illustration of this, we calculated the costs of a T cell transduction (TCT) run based on the stated minimal and typical, as well as the actual activities of our MACS® GMP IL-7 and IL-15 cytokines and those from another supplier<sup>1</sup>. The activity values were determined with side-by-side testing.

**Note:** We present normalized values in this case study to prevent the identification of products based on their activity values. Our aim is to sensitize users to the need for direct side-by-side testing rather than to promote a particular product.

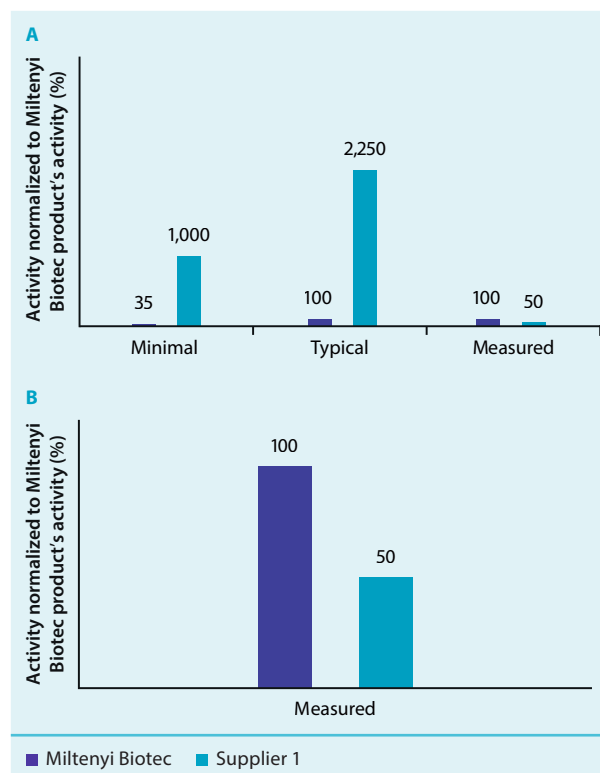
### Deviations from stated typical activities for clinical-grade IL-7 and IL-15

We tested our MACS GMP Cytokines and clinical-grade cytokine products from another supplier side-by-side in industry-standard assays for activity determination.



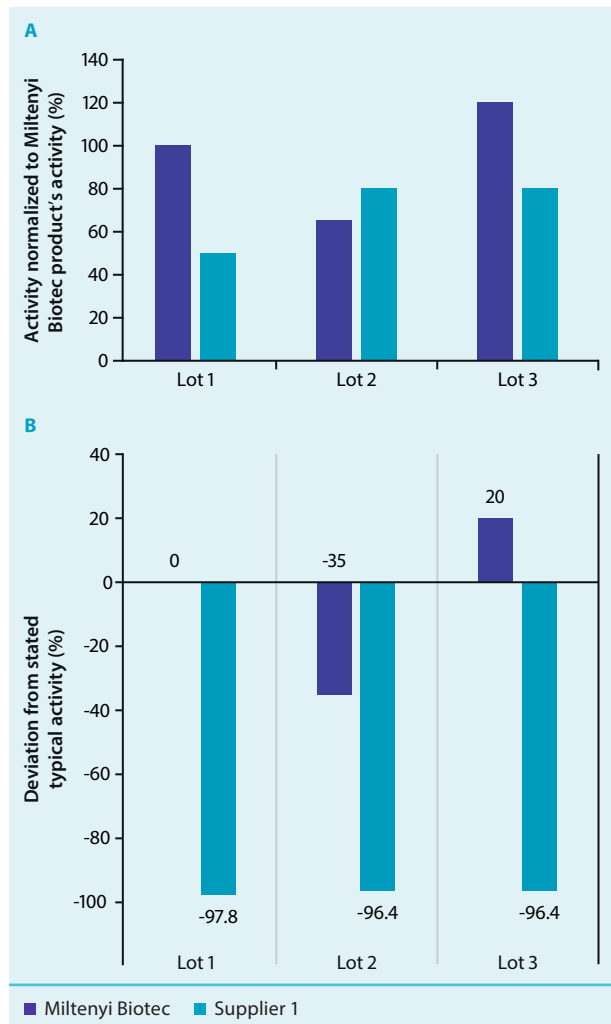
**Figure 1: An overview of the stated (minimal, typical) and measured activities for IL-7 products.** To prevent the identification of the other supplier's product based on their specified activity, all values are normalized to the activity measured for MACS GMP IL-7 (Miltenyi Biotec).

The measured activity of our MACS GMP IL-7 was roughly three times the specified minimal activity and slightly higher than the stated typical activity. The measured activity of the IL-7 from supplier 1 was only 50% of the stated typical activity (fig. 1). The measured activity of our MACS GMP IL-15 was roughly three times the specified minimal activity and corresponded very well to the stated typical activity. To our surprise, the measured activity of the competitor cytokine was 40-fold lower than the stated typical activity, reaching only ~2% of the value (fig. 2).



**Figure 2: An overview of the stated (minimal, typical) and measured activities for IL-15 products.** To prevent the identification of the other supplier's product based on their specified activity, all values are normalized to the activity measured for MACS GMP IL-15 (Miltenyi Biotec). (B) The measured IL-15 activities from A with a scale adjusted to the measured activities.

We confirmed our observations by testing two additional cytokine batches of the two IL-15 products and obtained comparable results. The IL-15 product from supplier 1 performed slightly better in the follow-up tests (3.6% of indicated typical activity in both experiments), but the overall deviation from the indicated activity remained consistent with the results observed in our initial test (fig. 3).



**Figure 3: An overview of the measured activity of different IL-15 product lots from Miltenyi Biotec and supplier 1.** To prevent the identification of the other suppliers, all values are normalized to the activity measured for MACS GMP IL-15 (Miltenyi Biotec). (A) The measured activities for 3 different lots of IL-15 products from Miltenyi Biotec and supplier 1. (B) The deviation of the measured IL-15 activities from the stated typical activities.

## Calculating the true cytokine costs for a TCT run

Based on the stated typical and observed performance data, we calculated the costs for clinical-grade cytokines for a TCT run assuming these recommended cytokine activities:

- IL-7 150–1500 U/mL
- IL-15 85–450 U/mL

A standard TCT procedure requires 6 liters of media, meaning the number of required units would be:

- IL-7  $9 \times 10^5$ – $9 \times 10^6$  U
- IL-15  $5.1 \times 10^5$ – $2.7 \times 10^6$  U

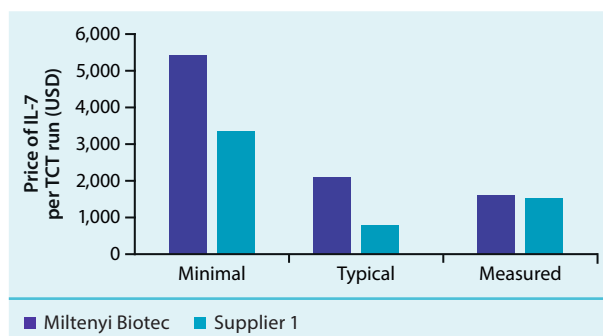
Using the high end of these recommendations, we calculated the total cytokine cost for the stated and measured activities for IL-7, IL-15, and both cytokines combined.

Based on the stated minimal activities for IL-7, the costs were USD 5,400 from Miltenyi Biotec and USD 3,344 from supplier 1. Based on the stated typical activities, the costs from Miltenyi Biotec dropped to USD 2,077 and the costs from supplier 1 dropped to USD 760.

However, when the costs were calculated using the values from the side-by-side measurements, the costs of MACS GMP IL-7 from Miltenyi Biotec were further reduced to USD 1,588, while those of the IL-7 from supplier 1 increased to USD 1,520 (table 1 and fig. 4).

IL-7	Price per run (USD)	
	Miltenyi Biotec	Supplier 1
Minimal	5,400	3,340
Typical	2,077	760
Measured	1,588	1,520

**Table 1: The price per TCT run for IL-7 from Miltenyi Biotec and supplier 1 based on the stated (minimal, typical) and measured activities for the cytokine.**



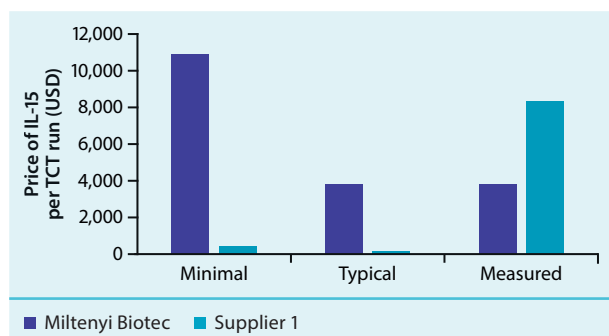
**Figure 4: Price per TCT run of IL-7 from Miltenyi Biotec and supplier 1 based on the stated (minimal, typical) and measured activities for the cytokine.**

Based on the stated minimal values for IL-15, the costs were USD 10,877 from Miltenyi Biotec and USD 415 from supplier 1. Based on the stated typical values, the costs from Miltenyi Biotec dropped to USD 3,807 and the costs from supplier 1 dropped to USD 185.

However, when the costs were calculated using the values from the side-by-side measurements, the costs of MACS GMP IL-15 from Miltenyi Biotec remained at USD 3,807, while those of the IL-15 from supplier 1 increased more than 40-fold to USD 8,305 (table 2 and fig. 5).

IL-15	Price per run (USD)	
	Miltenyi Biotec	Supplier 1
Minimal	10,877	415
Typical	3,807	185
Measured	3,807	8,305

**Table 2: The price per TCT run for IL-15 from Miltenyi Biotec and supplier 1 based on the stated (minimal, typical) and measured activities for the cytokine.**

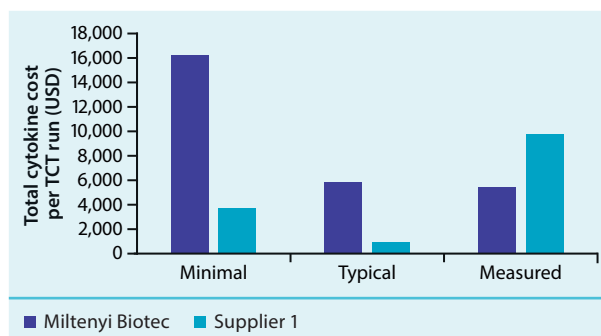


**Figure 5: Price per TCT run of IL-15 from Miltenyi Biotec and supplier 1 based on the stated (minimal, typical) and measured activities for the cytokine.**

The same calculations were applied for the total costs (table 3 and fig. 6).

Total	Price per run (USD)	
	Miltenyi Biotec	Supplier 1
Minimal	16,277	3,760
Typical	5,884	945
Measured	5,395	9,825

**Table 3: The price per TCT run for IL-7 and IL-15 from Miltenyi Biotec and supplier 1 based on the stated (minimal, typical) and measured activities for the cytokine.**



**Figure 6: Price per TCT run of IL-7 and IL-15 from Miltenyi Biotec and supplier 1 based on the stated (minimal, typical) and measured activities for the two cytokines.**

## Conclusion

The true costs of a TCT run can significantly deviate from the estimated costs. In our example, the deviation in measured versus stated typical performance of IL-15 and IL-7 of supplier 1 would result in underestimating the cost by a factor of ~10. Calculations based on minimal activities provided by Miltenyi Biotec would result in overestimating the costs by a factor of ~3. Given the huge volumes required in the development and manufacturing of clinical-grade cellular products, such deviations can have huge financial implications.

The stated typical activity for clinical-grade cytokines is not sufficient to accurately describe the real performance of a cytokine product. We therefore recommend comparing cytokines by evaluating their performance in the intended setting to make the best-informed decision. The application note "Your guide to side-by-side cytokine comparison" describes the process for side-by-side testing in more detail.

DOWNLOAD



Download our application note for side-by-side cytokine testing here:

► [miltenyibiotec.com/cytokine-testing](https://www.miltenyibiotec.com/cytokine-testing)



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<sup>1</sup>Cost calculations are based on prices in USD as of September 2021. Prices can vary in different countries. Please ask your local contact or distributor for a quote.

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