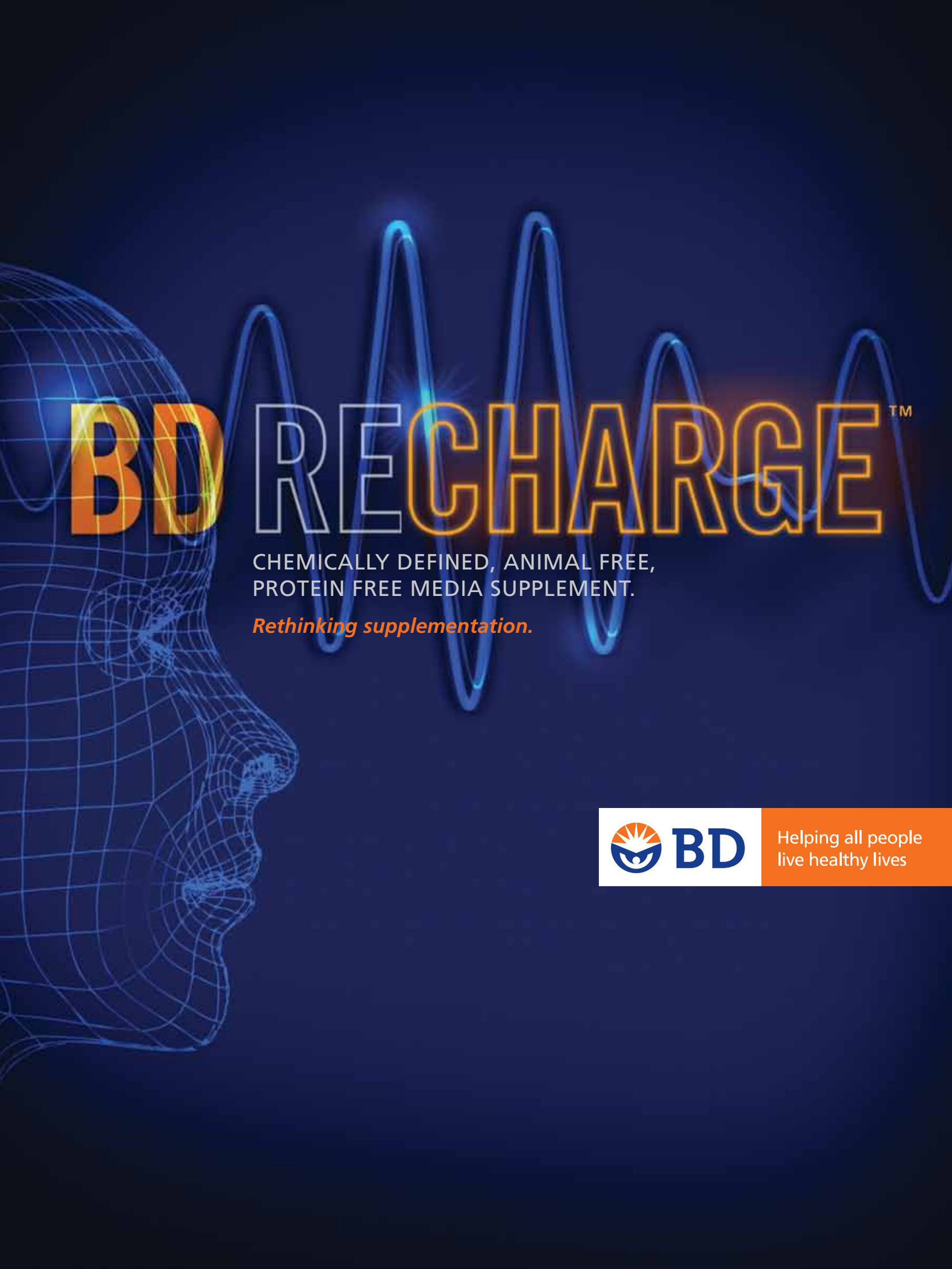

BD RECHARGE™
CHEMICALLY DEFINED, ANIMAL FREE,
PROTEIN FREE MEDIA SUPPLEMENT.
Rethinking supplementation.
BD
Helping all people
live healthy lives

INNOVATION.

With over 50 years of expertise in bacterial fermentation and mammalian cell culture, BD Biosciences – Advanced Bioprocessing products—including Difco™ and BBL™ brand supplements and media—are used as critical components in the production of some of the most widely used drugs and vaccines on the global market today.

BD continues to drive innovation through chemically defined supplements, that help boost performance, reduce risk and increase consistency. BD chemically defined supplements are designed to eliminate unnecessary constituents and potential inhibitors to maximize cellular activation and protein production. The result is protein quality and yield comparable to peptone supplementation — without the risks associated with undefined materials.

BD's animal free/antibiotic free (AF2™) facility sets a new standard for safety, quality and regulatory compliance for cell culture media. This new facility will manufacture products that are controlled for animal-origin component raw materials to the tertiary level — the most stringent level of control available, significantly reducing the risks associated with mixed-use facility.

At BD we're rethinking cell culture media and supplementation so you can redefine consistency and reduce risk within your manufacturing process. Visit www.bdbiosciences.com/advbio to learn more.

The first stand-alone, *dedicated, animal free, antibiotic free (AF2™) production facility for the cGMP production of high performance cell culture media and supplements.*

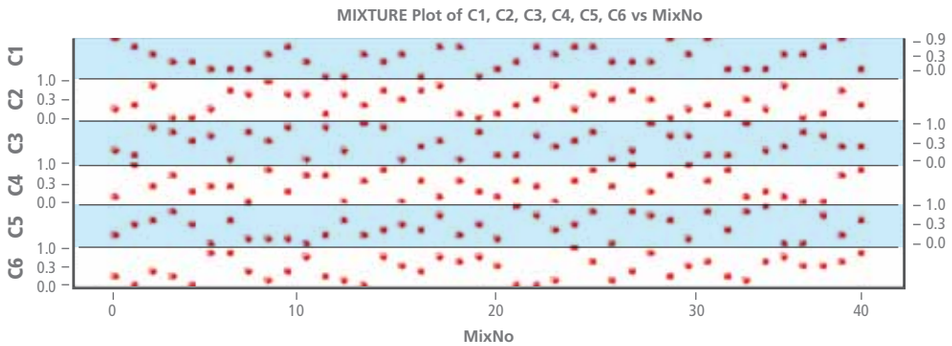
NEXT GENERATION SUPPLEMENTS:

Boost performance, Reduce risk, Increase consistency.

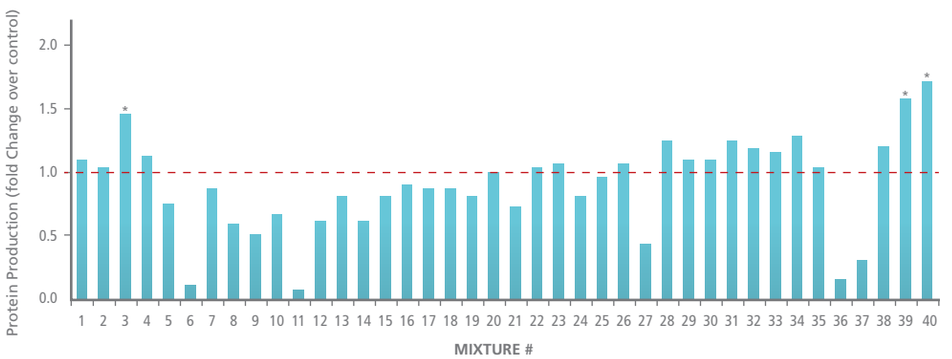
CHEMICALLY DEFINED.

Leveraging a half century worth of cell culture experience, next generation supplements are developed through the rigorous study of the properties of existing, proven supplements. Using proprietary fractionation processes, extensive analytical methods and relevant bioassays, key bioactive and nutritional components are identified. Iterative Design of Experiments (DoE) methodology is then used to select and combine the optimal chemical constituents for cell nutrition, growth and production. The resulting chemically defined supplement contains only the required constituents for high performance. Chemically defined supplements are only labeled as such when every constituent has a defined molecular structure.

Chemically defined supplements *are optimized using iterative Design of Experiments (DoE) methodology.*



Example of an Experimental Design for optimization of six bioactive components (C1-C6), at three levels for each component. The relative component concentration is indicated on the y-axis of each row; the mixture numbers are indicated along the x-axis.



*Effect of DoE Mixtures shown above on protein production. Data are presented as fold change in protein production of a luciferase-producing CHO cell line over negative control (medium only, dotted line) on day 12. *indicate mixtures with improved performance.*

RETHINKING SUPPLEMENTATION

YIELD AND PRODUCTIVITY.

Increased market acceptance and demand for biopharmaceuticals has led to advances in biopharmaceutical manufacturing processes and a need for incremental gains in yield and protein productivity of available cell lines. BD Biosciences Advanced Bioprocessing has been at the forefront in the development of tools and products that achieve higher protein productivity over traditional basal media. Improved base media supplementation and feeds continue to produce higher cell densities and higher viability across cell culture processes. By developing a chemically defined supplement that is an optimized formulation of nutritional and bioactive components, BD Biosciences' next generation supplements provide equivalent or better yield and productivity to peptone supplementation without sacrificing safety and speed to commercialization.

BD Biosciences is rethinking every aspect of biopharmaceutical manufacturing to reduce risk, accelerate time to market and deliver higher yield.

PROTEIN QUALITY.

Beyond creating environments where protein yield meets or exceeds that of current technology, it is important that the proteins produced using next generation supplements deliver the *right* therapeutic proteins. BD Biosciences Advanced Bioprocessing next generation supplements are developed to deliver not only high yield, but comparable protein quality to those produced using traditional supplementation methods.

CONSISTENCY.

Peptone supplements, derived from organisms such as plants or yeast, can have a composition which can statistically vary from one preparation to another. In a manufacturing operation that strives for standardization and reproducibility, such biological variability of the peptone components is a reason to innovate towards more consistency. With next generation chemically defined supplements this component variability is dramatically reduced.

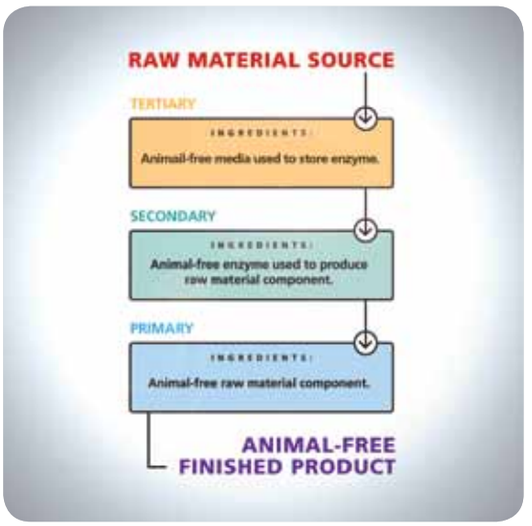
SPEED TO MARKET.

Through the elimination of undefined components, regulatory burden is reduced and approval processes streamlined, allowing for the acceleration of biopharmaceutical commercialization.

DEFINING ANIMAL FREE SAFETY.

Until now, no industry standards exist regarding the definition of "Animal Free," leaving you to try and discern the level of control your supplier may exert on your materials and manufacturing process. With BD Biosciences Advanced Bioprocessing, a new standard has emerged, whereby raw materials will be controlled to a tertiary level; the most stringent level of control available. This standard is defined as all ingredients, ingredient components and ingredient subcomponents utilized in production are not of animal origin.

All manufacturing and packaging equipment is dedicated and exclusively used for animal free products in a dedicated facility. And no historical, current or future animal source material or antibiotic use would be associated with the production facility. By defining "animal free" to the strictest of standards, BD Biosciences provides unparalleled assurance to your process and products.



Animal free *to the tertiary degree, from raw material source through to finished product.*

BD RECHARGE™ MEDIA SUPPLEMENT.

CHEMICALLY DEFINED. ANIMAL FREE. PROTEIN FREE.

The first in a line of next generation, chemically defined (CD), animal free supplements for the manufacture of biopharmaceuticals, BD Recharge can help you boost performance, reduce risk, and increase consistency. It is recommended for CHO cell lines that are responsive to yeast based supplements.

BD Recharge includes only key bioactive and nutritional constituents of yeast peptone to maximize cellular activation and protein production. This eliminates unnecessary constituents and potential inhibitors. The result is exceptional protein quality and yield comparable to peptone supplementation without the risks associated with undefined materials.

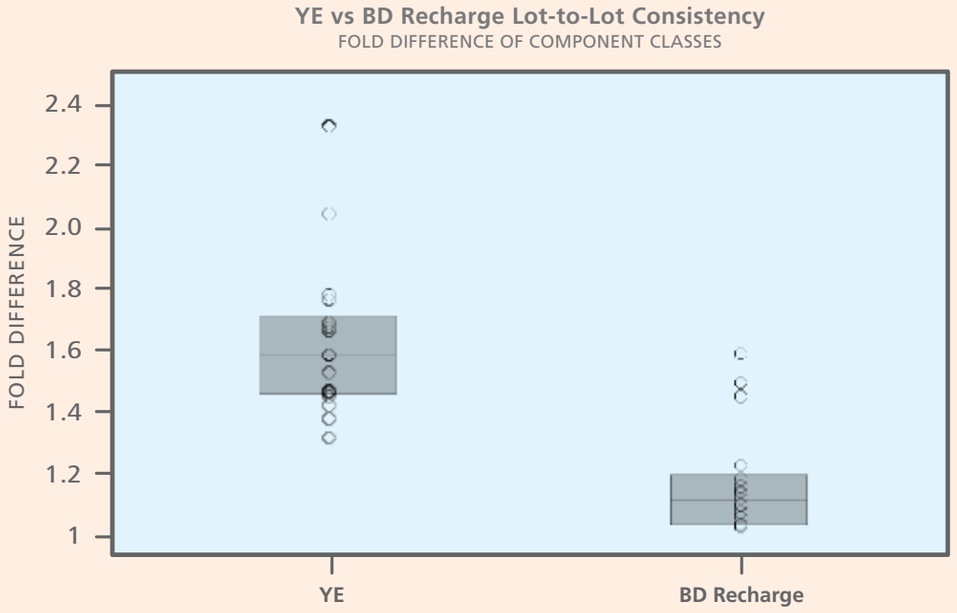
CONSISTENCY.

As a chemically defined formulation, the BD Recharge supplement is subject to far greater lot-to-lot component consistency than yeast based or other peptones.

Consistency in process raw materials can improve consistency in manufacturing processes. In turn, improved manufacturing process can result in efficient in process equipment utilization, reduced batch failure rates and reduction in overall manufacturing costs.

Component variability *of a yeast extract supplement vs. BD Recharge, multiple lots of yeast extract (YE) peptone and BD Recharge were tested for the variability of their component classes.*

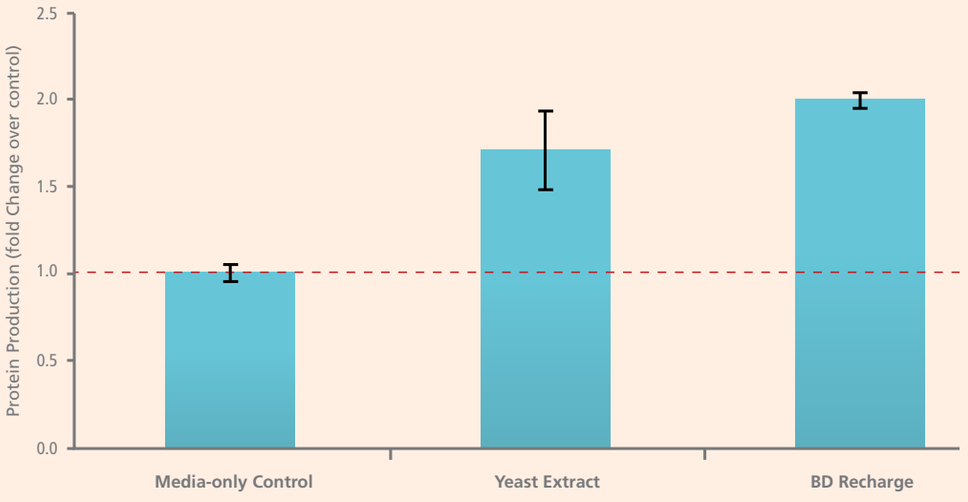
Results: *From one lot to another, BD Recharge was far more consistent in its chemical composition than YE peptone.*



HIGH PROTEIN YIELD.

Biopharmaceutical manufacturers have been reluctant to abandon peptone supplements made from meat, yeast and soy, despite the risk of lot-to-lot variability and regulatory burden, because of their high protein yields. BD Recharge is the first CD supplement that combines the productivity of peptone with the predictability, low risk, and regulatory simplicity of CD.

BD Recharge typically achieves comparable or greater protein yield to yeast based peptones and outperforms other commercial CD supplements.



Protein yield of cells supplemented with BD Recharge vs Yeast Extract
CHO cells expressing a recombinant monoclonal antibody were supplemented with either Yeast Extract or BD Recharge. Protein yields from these conditions were compared to CHO cells grown in the base media without supplementation. BD Recharge supplemented cells produced equal to or better than the yeast extract supplemented CHO cells.

BD RECHARGE™ IN YOUR PROCESS.

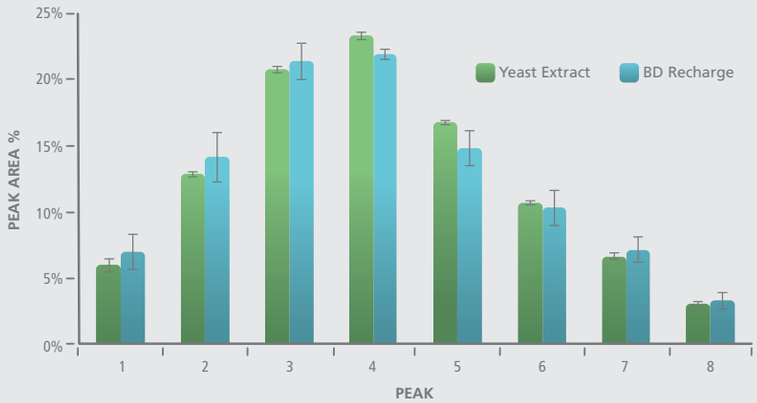
The transition from peptone supplements to BD Recharge CD supplement is a straightforward process. Because BD Recharge was designed to emulate yeast peptones, biopharmaceutical manufacturers can utilize it as a direct substitute with little to no adaptation required.

REDUCED RISK.

The elimination of undefined components significantly reduces risk of process related impurities associated with complex biologicals. Furthermore, BD Recharge is manufactured in BD Biosciences' new stand-alone, dedicated "Animal Free/Antibiotic Free" AF2 facility. The AF2 facility sets a new standard of control, guaranteeing that raw materials are animal-free to the tertiary level.

PROTEIN QUALITY.

Biopharmaceutical manufacturers are concerned not only with protein yield but also with quality. One measure of protein quality is the charge profile of the manufactured protein. In a chromatographic study, the quantification of the areas under the peaks of both sets of proteins should be comparable. The charge profile of the BD Recharge CD supplement is virtually identical to the yeast based peptones they replace.

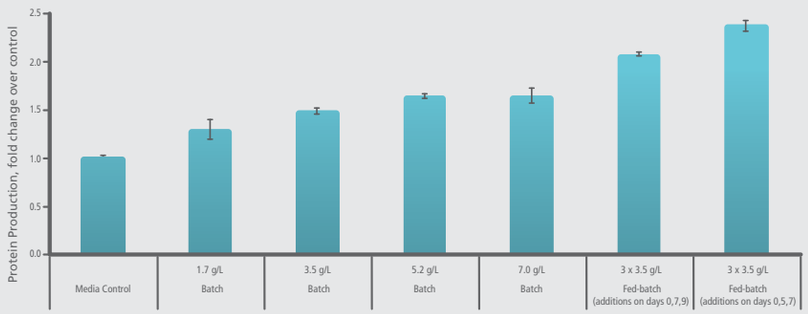


Protein quality of BD Recharge vs. Yeast Extract *Proteins produced with BD Recharge and a yeast extract peptone supplement were subjected to chromatographic analysis.*

Results: *For all eight peaks, the charge variance of the proteins produced with BD Recharge was similar to those produced with yeast extract. The chromatographic profiles of the proteins produced with the two supplements were virtually indistinguishable.*

EASY IMPLEMENTATION.

Testing has found BD Recharge to be effective with multiple base media, including customer-developed in-house media. BD Biosciences recommends use of a CD medium that supports growth of the target cell line. BD Recharge is compatible with both batch and fed batch processes.



REGULATORY BENEFITS.

As a chemically defined, animal free, protein free supplement, BD Recharge is ultimately expected to reduce customers' regulatory burden. BD Biosciences' regulatory support is available to help support customers in their filing process and by referencing the BD Recharge DMF (Drug Master File), approval is further streamlined.

ORDERING INFORMATION

Description	Catalog #	Quantity
BD Recharge™ w/o Glucose and L-Glutamine	670002	100 g bottle
BD Recharge™ w/o Glucose and L-Glutamine	670003	1 Kg pail
BD Recharge™ w/o Glucose and L-Glutamine	670004	5 Kg pail

For more information, visit bdbiosciences.com/go/recharge, call BD Technical Service & Support at 800.638.8663 or contact your Bioprocess Application Specialist.

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