BioProcess™ INTERNATIONAL

Using Animal-Free Peptones in Biopharmaceutical Production Processes

Reprinted with permission from BioProcess International 4(7):11-13 (July/August 2006)

In the biopharmaceutical industry, the requirement for animal-free processes that produce increased protein yields has prompted investigation into alternative forms of supplementation. Many companies have been very successful in meeting this requirement through the development of robust processes that include the use of animal-free peptones. To achieve this type of success, it is necessary to empirically determine which peptone works best in a particular process.

With the number of peptones available, it is necessary to include a wide variety of products in the screen. Because every peptone is different, multiple peptones produced using the same base material should be included. The number of peptones in the screen can be narrowed through an understanding of the process requirements. For example, if a low endotoxin level is required, the screen should be limited to only ultrafiltered (UF) peptones. Also, if the cell line uses the glutamate synthetase (GS) expression system, wheat peptones might be excluded from the screen because of their glutamine-rich composition.

Prior to initiation of the peptone screen, it is essential to select the base medium that will be used in the process. The base medium plays a major role in determining the success of a peptone screen, so it is critical to select a base medium that performs well in the production process. After the base medium is determined, the peptone screen should be designed so that each peptone is evaluated at a variety of concentrations. Cell performance will be different for each peptone and base medium combination, making it critical that a number of concentrations are evaluated for each peptone. This will ensure that the concentration yielding peak performance will be identified (Figures 1 and 2). Blends of peptones should also be considered, because synergistic effects have been observed in some processes when multiple peptones were used (Figure 3). Selection of the peptone or blend of peptones should be based on both the proliferation and production data, because these two parameters do not always correlate in a production process.

Once the peptone supplementation is determined, how the supplementation is applied should be considered. Although some processes require that a peptone is present from the beginning of the run, others perform best when the peptone is added as a feed later in the process. In some cases, optimal performance is achieved when the process begins with one peptone then another is added as a feed later in the production run. Feed development is an important part of any process, so it is critical to understand

Figure 1: TC yeastolate UF titration CHO line #1 in complete medium #1

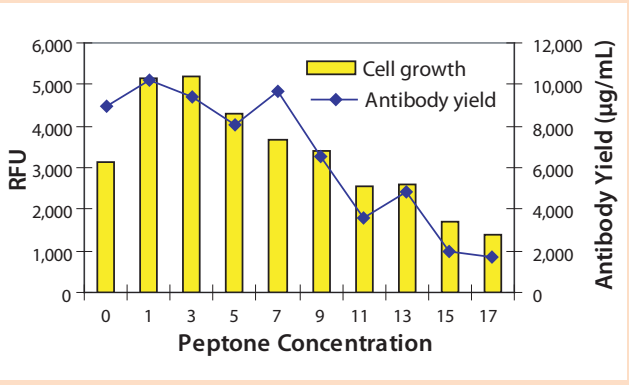

Figure 2: Wheat peptone UF titration CHO line #1in complete medium #1

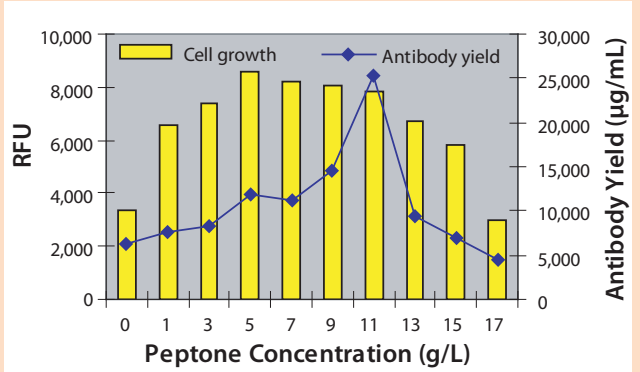

Figure 3: CHO line #1peptone blends in complete medium #1 shaker study production data

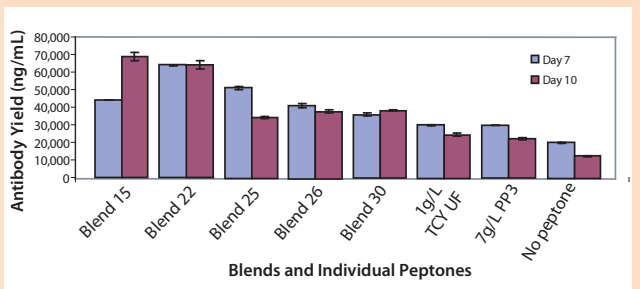

Figure 4: CHO line #2 bioreactor production and proliferation 3 g/L TC yeastolate UF fed on day 5

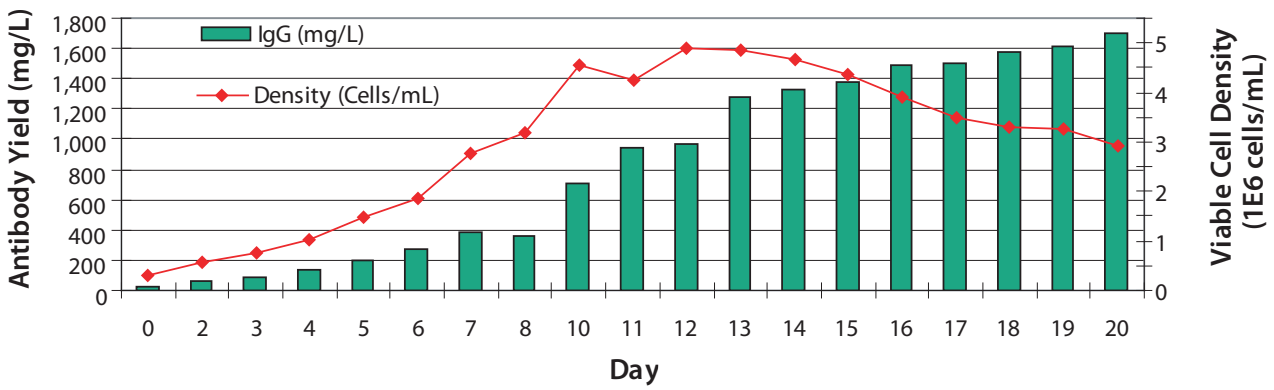

Table 1: BD peptones for cell culture

Product	Substrate	Catalog Number
Phytone™ Peptone	Soy	454 g — 211906 10 kg — 292450
Phytone™ Peptone UF	Soy	500 g — 210931 10 kg — 210936
Select Soytone	Soy	500 g — 212488 10 kg — 212489
Bacto™ TC Yeastolate	Yeast	100 g — 255772 10 kg — 255771
TC Yeastolate UF	Yeast	500 g — 292804 10 kg — 292805
Wheat Peptone UF	Wheat	In development
Bacto™ Yeast Extract	Yeast	500 g — 212750 10 kg — 212730
Yeast Extract UF	Yeast	500 g — 210929 10 kg — 210934

the nutritional requirements of the cells at every point of the process. With understanding the cell's requirements, it becomes possible to design a peptone feed strategy that greatly enhances the process performance (Figure 4).

Animal-free peptones have been successfully used throughout the biopharmaceutical industry to address increasingly stringent process requirements. By using the right peptone and base medium combination with the addition of the right peptone feed, a production process can be significantly improved. Development of a robust process requires use of a comprehensive screen and the selection of a good base medium.

To help with this development process, BD has a wide variety of animal-free peptones developed specifically for use in the biopharm industry. Additionally, because process development can be very time consuming, BD offers the AutoNutrient™ Media Design Service (AMDS) to expedite the development process. BD scientists work with customers from scale-up to full scale manufacturing for their tissue culture media needs to maximize productivity.

Stacy Holdread *is senior scientist in Research and Development at BD Diagnostics, 7 Loveton Circle, Sparks, MD 21152-0999; 1-800-638-8663; stacy_holdread@bd.com; www.bd.com/ds*

This article appeared in the Winter 2006 edition of *BD Catapult*.

BD™ Bionutrients

Animal-Free Peptones and Media

The Right Choice for Cell Culture and Fermentation

When you need a manufacturing partner that is:

- Industry focused
- Regulatory compliant and has
- Dedicated animal-free manufacturing capabilities

you need BD and our animal-free peptones and media. Backed by the long-standing expertise of Difco™ and BBL™ brand media, BD Bionutrients make the perfect choice to boost your production yield.

Animal-Free Products	Cat. No.
TC Yeastolate UF	292805
TC Yeastolate	255771
Yeast Extract	212730
Yeast Extract UF	210934
Yeast Extract LD	210941
Yeast Nitrogen Base	239210
Yeast Nitrogen Base w/o Amino Acids	291930
Malt Extract	218610
Phytone™ Peptone UF	210936
Phytone™ Peptone	292450
Select Soytone	212489
BD™ CHO Medium, w/o L-glutamine	220229
BD™ Cell MAb Medium, Animal-Free	220513

BD

BD Diagnostics
800.638.8663
www.bd.com/industrial