Nu-Tek BioSciences

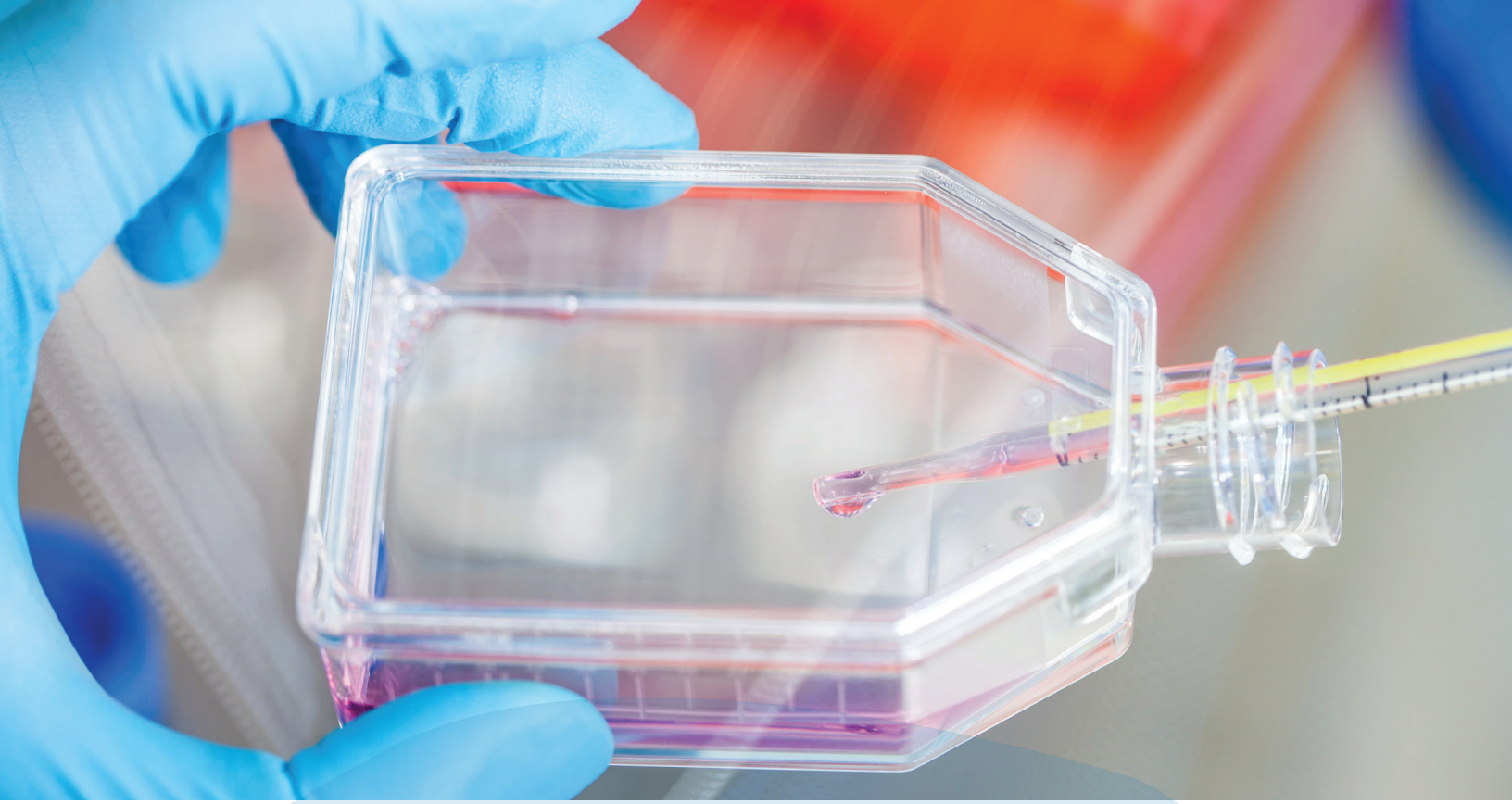
Fueling Cells Animal Free

# Cell Culture Media and Cattle:

## How Historic Lows in Livestock Will Impact the Future of Biotechnology Manufacturing

# Key Points

1. **Cell culture media relies heavily on animal-derived products,** particularly ingredients derived from cattle.
2. **Declining cattle populations will cause significant bottlenecks in the cell culture media supply chain for the next several years,** risking development and production of critical therapeutics.
3. **Nu-Tek's plant- and yeast-based peptones provide a viable alternative to animal-based supplements,** de-risking the biopharmaceutical development pipeline and reducing dependency on animal-based products.



## Overview

**Cell culture media, the nutrient-rich broth sustaining cells producing today's critical therapeutics, traditionally rely on animal-derived ingredients to promote and sustain cellular growth.** A significant portion of culture media in use today relies on access to healthy calves and cattle, whose blood and other components provide the base for the nutrient slurry required by cells to proliferate. However, the reliance on cattle ingredients is experiencing significant challenges to availability of supply, which has far-reaching consequences for the biotechnology sector.

**The U.S. cattle population has plummeted to its lowest level in decades,** with herds shrinking annually due to drought, rising feed costs, and market pressures.[1,2] While this decline poses immediate challenges for the agricultural sector, its ripple effects extend into biotechnology. Cattle-derived components like Fetal Bovine Serum (FBS) and casein underpin cell culture media - a $1.8 billion industry critical for drug development, including but not limited to vaccine production, monoclonal antibodies, and stem cell therapies.[1] For biotechnology leaders, connecting the declining cattle population to manufacturing – and finding ways to circumvent upcoming shortages – could mean the difference between production success and failure.

## Cattle's Role in the Cell Culture Media Industry

Cattle provide a variety of ingredients used in culture media. Fetal Bovine Serum, or FBS, is a cornerstone component used widely in the biotechnology industry and remains the gold standard in supporting cell cultures vital to developing and producing critical therapeutics. FBS is extracted from unborn calf blood and comprises a rich mix of growth factors, hormones, and proteins.[1] Beyond FBS, bovine plasma, collagen, Bovine Serum Albumin (BSA) and casein-derived materials are integral to specialized media. Cattle-based products in cell media allow for protein stabilization and prevent cell clumping; other products, such as collagen hydrolysates, provide the structural support needed for 3-dimensional cell culture growth. These components have historically dominated the cell culture industry due to availability and cost-effectiveness, with the global FBS market alone valued at nearly US $1.1 billion in 2024.[3]

## Direct Impact on FBS Production

A 5% decline in U.S. cattle herds (2023–2025) could reduce FBS output by 30–50%, as only 0.1% of slaughtered pregnant cows yield high-quality serum.[1,2] This scarcity has driven FBS prices up by 15–20% annually since 2023, straining budgets for academic labs and biomanufacturers.[4] Additionally, there are ethical and regulatory pressures surrounding the use of FBS and other cattle-based products; FBS collection involves cardiac puncture of bovine fetuses without anesthesia, raising animal welfare objections, and safety risks for products used to generate human therapies, as FBS batches risk contamination with prions, viruses, or endotoxins, complicating regulatory compliance.[5,6] With ethical, regulatory, and in some cases, sustainability challenges converging with declining cattle populations, alternative cell culture nutrient ingredients are needed – particularly as the biotechnology industry continues its near-exponential growth.

# Animal-Free Cell Culture Ingredients as Innovative Alternatives

Plant- and yeast-based ingredients are replacing animal-derived components in cell culture media, offering biopharmaceutical manufacturers a reliable, nutrient-rich solution for microbial and mammalian cell cultures without contamination concerns associated with animal-based products. Yeast extracts and peptones provide essential bioavailable peptides, amino acids, minerals, and vitamins.[7] These ingredients match or exceed the nutrient profiles of traditional animal-derived media, supporting robust cell growth and high-yield production of therapeutic proteins, monoclonal antibodies, and viral vectors.[8] For example, filtered yeast extracts have demonstrated superior performance in CHO cell cultures, achieving earlier peak cell density and higher product titers compared to chemically defined media alone.[8] Plant-based transferrin substitutes and yeast-derived nucleotides further eliminate reliance on bovine albumin or serum, ensuring consistent nutrient availability without batch variability inherent to animal sources.[9]

The shift to plant- and yeast-based media reduces critical risks in bioprocessing. Animal-free components eliminate exposure to prions, endotoxins, and viral contaminants-common in FBS-that can compromise cell lines or downstream products.[5] Additionally, plant supply chains are less vulnerable to disruptions than cattle-dependent systems, where even a 5% herd decline could slash FBS output by 30–50%.[10] This reliability is vital for large-scale biomanufacturing, where uninterrupted media supply ensures compliance with regulatory standards and accelerates time-to-market.[10] By leveraging scalable agricultural feedstocks and standardized fermentation processes, these alternatives provide cost-effective, sustainable solutions for therapeutic protein production while maintaining strict quality control and continuous access to a reliable material supply chain.[8]

Even with a historically low cattle population, some biotechnology manufacturers may wish to continue working with FBS to some degree or require its continued use. To offset rising product costs and lack of availability while maintaining quality of production, it is also possible to augment existing formulations to enable reduction in cattle-derived materials.

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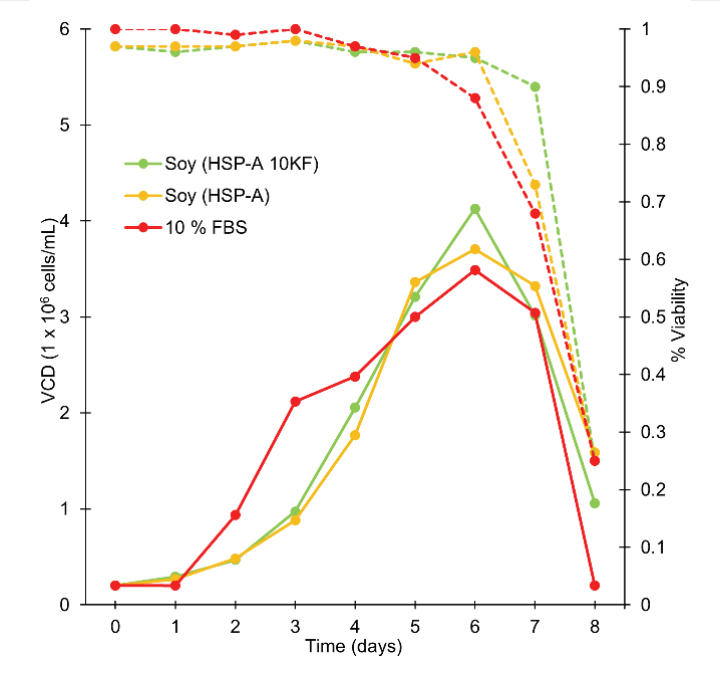
# CASE STUDY

# Enabling Animal-Free Formulations with Nu-Tek BioSciences

**Nu-Tek BioSciences produces plant- and yeast-based hydrolysates, extracts, and peptones for the biotechnology and pharmaceutical industry. Manufactured in its 100% animal-free, purpose-built, state-of-the-art facility in Austin, Minnesota (USA), Nu-Tek's products are used globally to produce breakthrough therapies in cancer treatments, vaccines, and other critical therapeutics.**

Nu-Tek's products are often used as the primary nutrient source for cell culture media, supporting bacterial, mammalian, and insect cell culture for research and development as well as commercial biomanufacturing. Nu-Tek's products can also be used to reduce or eliminate the use of existing animal-origin culture media ingredients, such as FBS, to decrease costs and risk without losing culture productivity. Below are case examples of replacement of cattle origin culture media ingredients with Nu-Tek's animal-origin-free products without productivity interruption.

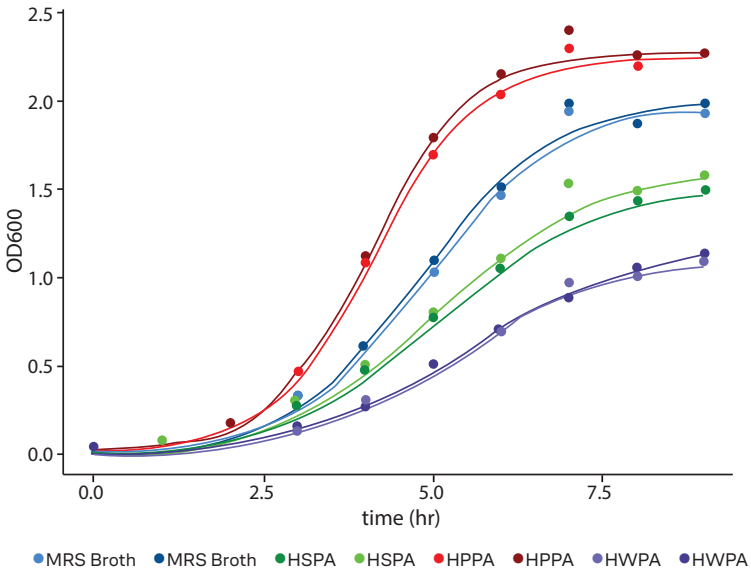
## Case Example 1: Successful removal of FBS from mammalian cell cultures.




CHO-K1 cells were transitioned to serum-free media containing 0.4% w/v Soy Peptone (Nu-Tek BioSciences, HSP-A or HSP-A 10KF). Under serum-free conditions, peak viable cell density (VCD) increased by 20% and the cell viability drop off was delayed by 24-48 hours.

## Case Example 2: Improved growth performance of *Lactobacillus lactis* under animal-origin-free conditions.

Duplicate cultures of *L. lactis* were propagated in MRS broth, containing either beef extract (blue; Criterion) or animal-origin-free alternatives, Soy Peptone (green; Nu-Tek BioSciences HSP-A), Pea Peptone (red; Nu-Tek BioSciences, HPP-A), or Wheat Peptone (purple; Nu-Tek BioSciences, HWP-A). The OD600 vs time plot demonstrates carrying capacity increased by 14% and intrinsic growth rate by 25% when grown in Pea Peptone compared to the beef extract-containing MRS broth.



## Case Example 3: Replacement of casein-derived components in classical microbiology media.

| Tryptose Soy Broth | *B. subtilis* | *E. coli* | *S. pyrogenes* | *S. epidermidis* |
|---|---|---|---|---|
| Tryptose (Casein) | **** | **** | **** | **** |
| Soy | **** | **** | **** | ** |
| Pea | **** | **** | **** | ** |
| Wheat | **** | **** | **** | **** |
| Cottonseed | ** | **** | ** | * |
| Yeast | **** | **** | **** | **** |

| Tryptose Phosphate Broth | *B. subtilis* | *E. coli* | *S. pyrogenes* | *S. epidermidis* | *S. pneumoniae* |
|---|---|---|---|---|---|
| Tryptose (Casein) | **** | **** | **** | **** | ** |
| Soy | **** | **** | **** | **** | **** |
| Pea | **** | **** | **** | ** | ** |
| Wheat | **** | **** | **** | **** | **** |
| Cottonseed | ** | **** | **** | — | — |
| Yeast | **** | **** | **** | **** | **** |

| | |
|---|---|
| **** | 1 days to reach full turbidity score |
| ** | 1 days to reach full turbidity score |
| * | 3 days to reach full turbidity score |
| — | Does not support growth |

Multiple bacterial strains, as indicated in the above tables, were cultured in classical microbiological media formulations, Tryptose Phosphate Broth (TPB) or Tryptone Soy Broth (TSB). Media was formulated with either casein-derived tryptose/tryptone or animal-origin-free peptones, including Soy, Pea, Wheat, Cottonseed Peptones or Yeast Extract. Soy and Wheat Peptone and Yeast Extract were able to broadly replace tryptose in TPB, including improved performance in the growth of S. pneumoniae. Wheat Peptone and Yeast Extract were able to broadly replace tryptone in TSB while maintaining growth performance across organisms tested.

# The Future of Animal-Origin-Free Cell Culture

**The decline of the U.S. cattle population - now at its lowest level since the early 20th century -poses a critical challenge to the biotechnology industry, which has long relied on animal-derived components like fetal bovine serum (FBS) for cell culture media.** Shrinking herds will challenge the current supply chain and threaten the affordability of biologics, vaccines, and therapeutic protein manufacturing. However, this crisis also underscores an emerging opportunity to adopt plant- and yeast-based alternatives, such as plant hydrolysates and yeast extracts, which provide comparable or superior nutrient profiles (peptides, amino acids, vitamins, and minerals) to FBS without animal-origin risks. These ingredients not only eliminate contamination concerns and batch variability but also offer scalable, sustainable solutions to augment or fully replace traditional media formulations.

By transitioning to animal-free nutrients or augmenting existing formulations to include plant-based materials, biomanufacturers can future-proof production processes, maintain cell culture productivity, and align with ethical and regulatory imperatives, ensuring resilient supply chains in an era of unprecedented agricultural disruption. Nu-Tek BioSciences is the market leader in providing premium plant- and yeast-based peptones, extracts and hydrolysates that can provide manufacturers with the nutrients needed to maintain or improve production without navigating the risks posed by animal-based ingredients.

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