



# Our position on ~~Bioengineering~~

The increased competition, especially among Asian industrial fermentation companies has led to serious modifications in the biosynthesis of menaquinone-7.

Within 2015 and 2024 there were 231 studies on “menaquinone fermentation” published on Pubmed. **Chinese authors took the lead with 101 publications**, leaving other countries far behind. The knowledge gap between producers and regulatory bodies continues to widen.

These advancements introduce potential uncertainties for food consumers, primarily due to the engineered and highly controlled processes that differ significantly from traditional fermentation. Here are the major concerns:

## Genetic Engineering of Strains

Using genetically modified *Bacillus subtilis* strains to enhance MK-7 production may raise safety concerns, especially regarding the potential for unintended side effects or allergenic responses. Consumers who prefer fermented products may find genetically engineered strains are unsettling, and there's the possibility of regulatory scrutiny due to the modified organisms.

## Metabolic and Synthetic Biology Approaches

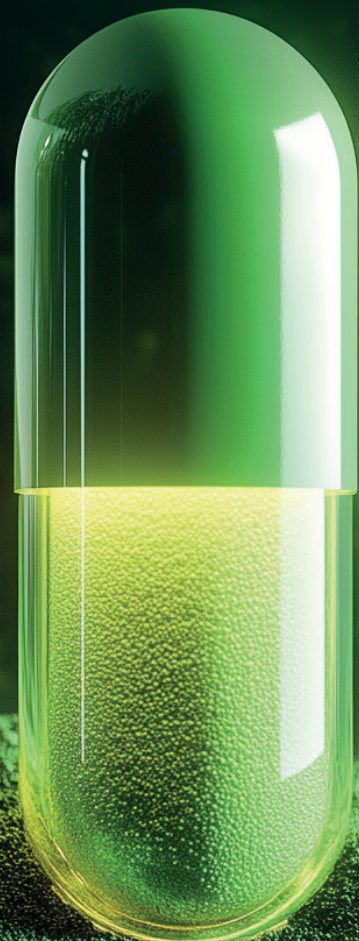
Techniques such as introducing cofactor regeneration systems and utilizing synthetic biology to manipulate metabolic pathways are also contentious. This high level of intervention in the microorganism's natural processes could alter the final product's safety profile or nutritional content, leading to concerns about the unknown long-term effects of consuming such products.

## Alternative Substrates and Industrial By-Products

The use of non-traditional substrates, including agro-industrial by-products, may introduce contaminants or residues, particularly if they are not food-grade. This raises concerns about the purity and safety of the resulting MK-7.

## Continuous Biofilm Fermentation

Continuous biofilm reactors increase yield and productivity but may also lead to bacterial adaptations or mutations over prolonged fermentations, potentially impacting the stability or predictability of the final product.





#### Organic Acids (e.g., Succinic Acid)

Organic acids, like succinic acid, are sometimes included to support the biosynthetic pathway, providing intermediates that can enhance MK-7 synthesis.

#### Cofactors (e.g., NADPH Regenerators)

Chemical cofactors or regeneration systems, like NADH or NADPH, are sometimes introduced to boost the activity of key enzymes in the MK-7 biosynthetic pathway. In synthetic biology contexts, cofactor recycling systems can be chemically optimized to provide a more constant supply of energy for enhanced production.

Some of these modern fermentation methods can incorporate **chemical substrates**, particularly in the optimization of fermentation media and enhancement of metabolic pathways. Some of the chemical substrates and additives commonly used include:

#### Isoprenoid Precursors

Some modern methods supplement the fermentation media with isoprenoid pathway precursors, such as farnesyl pyrophosphate or other isoprenoid intermediates, to promote the biosynthesis of menaquinone-7. These substrates act as building blocks, driving the downstream production of MK-7.

#### Chemical solvents are used to extract and purify MK-7 after fermentation.

Here are some common solvents involved: Hexane, Ethanol, Isopropanol, Methanol and Acetone. These chemical substrates and enhancers can increase the yield and efficiency of MK-7 production but may also contribute to concerns about the naturalness and purity of the final product.

The genetic engineering of strains, the use of synthetic biology and chemical solvents might be seen as going too far, especially for consumers seeking natural fermentation products. These methods push the boundaries of traditional processes by introducing non-native elements and heavily modifying the microbial metabolic pathways. This could create a perception of „unnatural” production and may warrant more research into safety implications, transparency in labeling, and regulatory oversight to address consumer concerns.

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