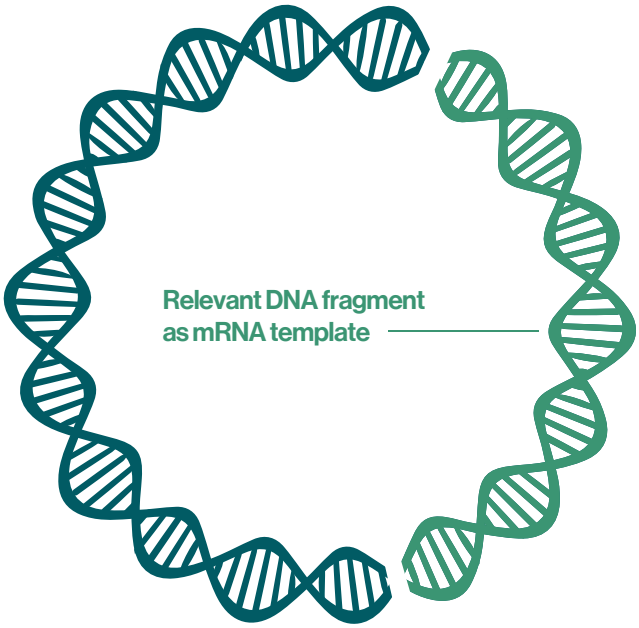
What is plasmid DNA?



Natural carrier of information:

Plasmids are small, ring-shaped DNA fragments that can occur in bacteria in addition to their genomic DNA.

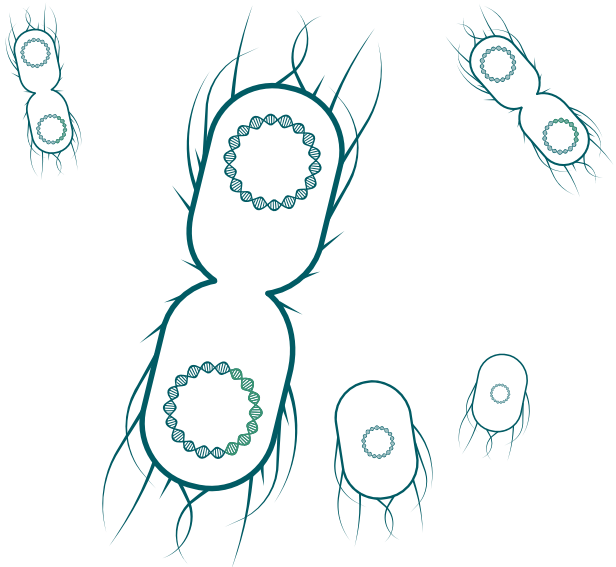
Additional biologic capabilities:

Plasmids often contain genetic information that can provide the bacterium with specific capabilities, such as antibiotic resistance.

DNA is required for mRNA production:

To produce mRNA, a DNA template is required. The biopharmaceutical industry uses plasmids for this purpose. A part of the plasmid DNA encodes for the relevant protein of interest, e. g. the spike protein of SARS-CoV-2. The majority of the plasmid is used to shape the DNA into the required ring form. The ring-shape is essential for the amplification of the relevant DNA sequence.

How does plasmid production work?

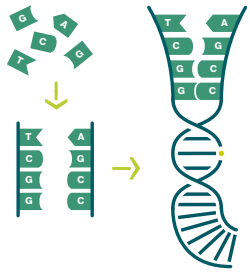


A biological copy machine:

During a bacterium's natural cell division, everything inside the single-cell organism is duplicated before the cell divides. This characteristic is used to amplify plasmid DNA. For this purpose, a plasmid is transferred into a bacterium so that identical copies of the plasmid are produced during the process of cell division.

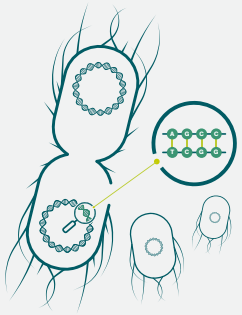
What role do plasmids play in the manufacturing of mRNA-based drugs?

01 Oligosynthesis



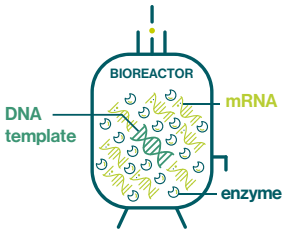
In this process, the blueprint for the desired protein of interest is created. For this purpose, nucleotides are lined up as building blocks that form a code. Two complementary single DNA strands are produced chemically, forming the familiar double helix structure. This DNA fragment is inserted into a plasmid that serves as a carrier.

02 Amplification



Plasmids are transferred into bacteria. During their cell division, the plasmids are also replicated. The relevant DNA fragments are isolated from the plasmids and cells. They form the template for mRNA transcription.

03 mRNA production

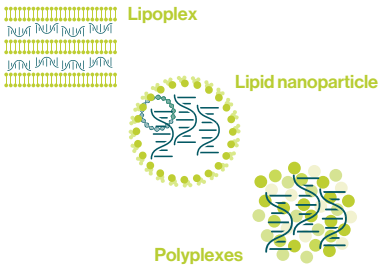


To produce mRNA, the DNA template is transcribed into mRNA in a bioreactor. This enzyme-based process is known as in-vitro transcription (IVT). More than 500 mRNA strands can be produced with a single DNA template obtained from a plasmid.

04 Purification and concentration

Following the mRNA production in the bioreactor, the mRNA is purified by a filtration process to remove product-related impurities. This purification process also includes the removal of DNA plasmids that are therefore not part of the final mRNA vaccines or therapeutics. After purification, the mRNA solution is contentrated and filtered again. The resulting solution is called drug substance (DS).

05 Formulation



The mRNA as the drug substance is combined with lipid nanoparticles (LNP). This step is called formulation and serves to protect the mRNA from degradation and ensure its delivery to the correct target cells when administered as a vaccine. The ready-to-fill vaccine is called Drug Product (DP).

06 Fill & Finish

The final manufacturing step is a sterile filtration and filling of the vaccine into vials. The vials are labeled and undergo a strict quality control before packaging.

About the Marburg site

BioNTech's site in Marburg is one of the largest manufacturing facilities for mRNA-based vaccines in Europe.

Employees:
Since its acquisition through BioNTech, the number of employees at the Marburg site has more than doubled (2020: approx. 300 people).

2022
approx. 700 people

Continuous investments:
BioNTech has continuously invested in the Marburg site; the number of total investments for the new manufacturing facility amount to

approx.
40 million euros

Strategic development plan for the Marburg site

Investments are part of a long-term development plan for the BioNTech site in Marburg, which covers four strategic areas in manufacturing:

01  Commercial production of the Pfizer-BioNTech COVID-19 vaccine since the beginning of 2021

02  A technology hub for innovative manufacturing solutions such as the BioNTainers, which encompasses the operation of the first two modular manufacturing units as prototypes

03  The manufacturing of mRNA vaccine candidates on a clinical scale to support clinical trials. The focus is currently on candidates from the Company's proprietary FixVac platform, in particular BNT111

04  Plasmid DNA manufacturing to produce a key starting material for mRNA- and cell-based drugs in-house

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