

NOMAD Bioscience Receives Its GRAS Regulatory Clearance In USA For Colicins Manufactured In *N. benthamiana*

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NOMAD Bioscience received a formal 'no questions' letter from the US Food and Drug Administration (FDA) in response to NOMAD's GRAS notice GRN 775 describing use of Colicins produced in plant species *Nicotiana benthamiana* as 'Food Processing Aids' for control of major foodborne pathogenic strains of *Escherichia coli*. Colicins are natural non-antibiotic antibacterial products developed by NOMAD. The FDA's response represents the third regulatory concurrence from the Agency that plant-made Colicins are safe to use on foods and it paves the way for industrial production of Colicins as novel antibacterial food additives. The first Nomad's submission (GRN 593) described the use of Colicins for control of major foodborne pathogenic strains of *Escherichia coli* for the post-harvest treatment of fruits and vegetables and the second one (GRN 676) described the use of Colicins as 'Food Processing Aids' on beef, pork and lamb meats; both earlier submissions also received a formal 'no questions' response from the reviewing agency. The current GRN 775 extends the list of plant manufacturing hosts allowed for Colicin production to include *Nicotiana benthamiana*, a non-edible species that is currently a standard manufacturing plant host for production of biopharmaceuticals. *N. benthamiana* is a very well researched plant manufacturing host, and its well characterized agronomy and physiology and its ability to accumulate very high levels of recombinant proteins make the plant an especially suitable host for biopharmaceuticals and food additives that have to be manufactured under highly controlled conditions and in compliance with the good agronomic and manufacturing practices (cGMP). The use of *N. benthamiana* as a manufacturing host also significantly improves manufacturing economics.

Because the efficacy of antimicrobials applied to US meats is under the jurisdiction of the US Department of Agriculture (USDA), the USDA's Food Safety and Inspection Service (FSIS) co-reviewed with FDA NOMAD's data package and concluded that Colicins produced in *N. benthamiana* meet USDA suitability criteria.

Enterohemorrhagic or Shiga toxin-producing *Escherichia coli* contaminating food products are a major cause of bacterial enteric infections in USA and worldwide. NOMAD's product candidates described in the application are simple mixtures of two or more bacterial Colicins produced in plants and applied at very low concentrations; the products are highly and broadly active against all major pathogenic *E. coli* strains causing food poisoning defined by USDA/FSIS as requiring priority control ('Big Seven').

In addition to Colicins, other plant-produced bacterial and bacteriophage antimicrobial proteins (Bacteriocins and Bacteriophage Lysins) are being developed by NOMAD as inexpensive food additives and food processing aids for the broad control of bacterial pathogens (*Escherichia coli*, *Salmonella enterica* and *Clostridium perfringens*) in food products. NOMAD is also actively developing Bacteriocins and Bacteriophage Lysins as medical alternatives to antibiotics, with its pre-clinical research focused on novel antibacterial proteins for control of major multi-drug resistant Gram-negative pathogens including *Escherichia*, *Pseudomonas* and *Klebsiella*.

About NOMAD Bioscience GmbH. Nomad Bioscience GmbH is a plant biotechnology company developing a broad range of biotechnology products manufactured in plants. Corporate offices are headquartered in Munich, Germany and the Company's Research Division is located in Halle, Germany. NOMAD Bioscience GmbH has two subsidiary companies: Nambawan Biotech GmbH (Halle, Germany) and UAB Nomads (Vilnius, Lithuania).