## The program of the comprehensive examination on

#### 19.04.01 Biotechnology

# Subject 1. Biotechnology as a science. The raw material base and hardware equipment of biotechnological industries.

Goal, objectives, and subject of biotechnology. Empirical, etiological, biotechnical and genes technology periods of the history of biotechnology development as a science.

Akaryotes, prokaryotes and eukaryotes like biotechnology facilities. Types of relationships between biological objects (symbiosis and antibiosis), examples. The relationship between biological objects in the process of symbiosis (commensalism, mutualism, neutralism), examples. The relationship between biological objects in the antibiosis (one-sided and two-side antibiosis), examples.

Total, specific and special methods used in biotechnology.

Characteristic of biotechnological produce, its main customers.

Peculiarities of control over biotechnological processes, levels of management. The dependence of control and management of biotechnological processes on the characteristics of production processes. The system of organizing pre-clinical testing of biologically active substances (GLP). Activities within the framework of common rules of GLP system. The system of requirements for the quality control of biologically active substances in industrial production (GMP). Characteristics of GMP system requirements for biotechnology and biological safety.

The legal base for the field of biotechnology.

The raw material base for biotechnology. Expensive raw materials, food industry and specially received raw materials for microbial synthesis. Nutritional substrates used in biotechnology: sugar alcohols, hydrocarbons, nitrogen compounds, substrates of indefinite composition. Intermediate products as raw material base for biotechnology.

Peculiarities of making formula of nutrient media for microorganisms cultivation.

Apparatus equipment for biotechnological production. Types of biological reactors. Bioreactors with mechanical, pneumatic and circulation mixing, their characteristics, purpose. Requirements for biological reactors. Laboratory, pilot and industrial biological reactors. Process of scaling in industrial bioreactors.

Classification of biotechnological processes according to the nature of biological object, generality and specificity of processes, the number of biological objects, the terms of the process, the stages of production technology realization of target products, the mechanism of formation of desired product, management process, and the type of biotechnological process.

Phases of microbial cells growth: lag phase, log phase, the phase of growth slowing, stationary phase.

Mass and heat exchange in biotechnological processes. Oxygen transfer rate. Factors affecting rate of oxygen consumption by biological object. Thermostating of enzymatic process. Equation describing heat exchange. Methods for increasing heat exchange rate.

Foaming and foam extinguishing. Causes of foaming in bioreactor. Mechanical, acoustic and chemical foam coolers.

Preparing sterile air and purifying exhaust air. Filters for coarse and fine purification. The main technological stages for sterile air preparation. Methods for cleaning exhaust air: the method of catalytic post-combustion, the method of liquid-phase oxidation, screen filters application method.

Characteristics of some types of biotechnological processes: turbidostately and stately cultivation modes, repeating and continuous culture modes, solid, surface, and gas-phase fermentation, and others.

The technique of biotechnological products isolation out of the cell mass and culture fluid. Separation of biomass from the cultural liquid (flotation filtration, ultracentrifugation). Physical, chemical and chemical enzymatic methods of cell disruption. Isolation of products from cell biomass and culture fluid: precipitation, extraction, adsorption. Modern methods of product separation (chromatography, electrophoresis). Varieties of chromatography: ionic exchange chromatography, gel filtration. Electrophoresis modifications: two-dimensional electrophoresis, electrophoresis in a heterogenous electric field, isoelectric focusing, immunoelectrophoresis, isotachophoresis. Methods of concentration of biotechnological products: reverse osmosis, ultrafiltration, evaporation. Dehydration, modification and stabilization of products. Obtaining commodity forms of drugs.

# Theme 2: Selection of microorganisms. Basics for genetic engineering of microorganisms. Immobilization of enzymes.

Peculiarities of microorganisms as objects of selection. Principles of microorganisms selection: mutational variation, selection of positive mutants, hybridization of microorganisms. Methods of preservation and conservation of a producing strains activity.

Maintaining purity of the culture and fight against microbe contaminants. Membrane filtration: filter types, advantages and disadvantages, the purpose of their usage. Heat sterilization: periodic and continuous sterilization, advantages and disadvantages, purpose. Autoclaving.

Methods of genetic engineering in biotechnology. Gene, genomic and chromosomal engineering. Tasks of genetic engineering. The technology of recombinant DNA. Methods for preparing fragments of foreign DNA and their purification. Enzymes for rDNA. Sequencing. Vectors in technology of rDNA

types, requirements to them. General scheme of construction of rDNA genes and cloning. Preserving recombinant DNA.

Amplification of genes. Polymerase chain reaction, its characteristics. Genes expression. Technological scheme of cloning and genes expression. Genomic library, what it means. Hybridous technology, its definition and stages.

Features and benefits of immobilized enzymes. Carriers for immobilizing enzymes: claims, organic and inorganic carriers. Methods of physical immobilization of enzymes: adsorption on insoluble carriers, inclusion into the pores of gel, the separation of the enzyme from the rest of the medium semipermeable membrane, including in a biphasic reaction medium. General characteristic of chemical immobilization of enzymes. Basic techniques of chemical immobilization of enzymes: the reaction of amide bonds formation, reaction of formation of urea bonds, the reaction of secondary amine formation, thiol - disulfide exchange reactions.

# Subject 3. Microbiological production of amino acids, proteins, enzymes and organic acids

Types of cell metabolism products, examples, value in biotechnology industry. Enzyme and gene regulation of synthesis of primary and secondary metabolites, regulation by metabolites. Prospects for the usage of biomass.

Yeast, bacteria, algae, fungi as a non traditional source of protein. Paraffin oil, methanol, ethanol, plant biomass, etc., as a raw material for synthesis of single-cell protein. Process diagram of growing fodder biomass.

The main stages of deep and shallow methods of cultivating of enzyme producers. Advantages and disadvantages of various methods of cultivating enzyme producers. Technology for producing purified enzymes. Areas of industrial application of microbial enzymes.

Producers characteristic and the general principles of mass microbiological production of L-glutamic acid and other amino acids. Single-stage and double-stage processes for the preparation of amino acids.

Anaerobic and aerobic processes of producing organic acids. Technological scheme of obtaining L (+) - lactic acid, characteristic of producers. Obtaining citric acid: characteristic of producers, superficial way of liquid-phase fermentation, solid state fermentation, underlying way. Mass microbiological production of propionic, gluconic, itaconic, and malic acid.

### Theme 4. Agricultural and Environmental Biotechnology

Biotechnology in animal husbandry. Methods for ensilage of green mass of plants. Characteristic of silage microflora. Chemical and microbiological processes occurring during ensilage. Chemical, enzymatic and bacterial preparations for ensilage of fodder.

Principle of producing haylage . Technology of haylage preparation Microbiological and biochemical processes occurring while producing haylage. Theoretical bases for producing haylage.

Feed additives of biotechnological origin: forage amino acid preparations, enzyme preparations, vitamins, probiotics, wastes of alcohol, brewing, sugar beet and other industries.

Biotechnology of animal cells. Stages of cultivation of animal cells. Deep cultivation of animal cells in a monolayer and in suspension cultures. Nutrient medium for cultivation of animal cells.

Cell engineering in animal husbandry. Embryo transfer technology (example with cattle). Fertilization of eggs outside animal body. Methods for cloning animals.

Genetic engineering in animal husbandry. Methods for generating transgenic animals, microinjection of gene, transplantation of transfected nuclei, sperm use as vectors of the exogenous DNA. Breeding transgenic animals with new economic-useful properties and resistance to diseases. Application of transgenic technology to improve milk composition, with improved characteristics. Transgenic animals which produce biologically active substances for medical and technological applications.

Biotechnology in crop production. Advantages of bacterial fertilizers as compared with chemical means. Bacterial fertilizers based on symbiotic nitrogen-fixing bacteria (nitragin, rizotorfin). Bacterial fertilizers based on nitrogen-fixing non simbiotic Bactria (flavobakter, rizoenter, azotobacter, risobacter, ekstrasol et al.).

Vegetative propagation of plants by tissue cultures. Surface cultivation of plant cells. Cultivation of plant cells in subsurface conditions. Preserving cultures of plant cells.

Biological methods for plant protection. Bacterial entomopathogenic drugs. Fungal entomopathogenic drugs. Entomopathogenic viral drugs. Preparations for the protection of plants against pathogenic microorganisms (antibiotics, phytoalexins, microbes antagonists, vaccines and immunologic drugs). Phytoregulators in plant protection system.

The usage of genetic engineering in phytobiotechnology. Sexual and somatic hybridization of plant cells. Mechanical and biochemical methods for producing protoplasts of plant cells.

Bioconversion of agricultural wastes. Technological process of methane fermentation of manure. Degradation of organic substances in methanogenesis. Methane bacteria. Biogas production. Construction digesters. Production of organic fertilizers from waste products of agriculture, food industry and others.

Biological problems of conservation and restoration of environment. Thick, liquid and gaseous waste products of biotechnological industries. Recovery of

waste products of biotech industries. Aerobic outflow rectification system. COD. BOD. Extensive and intensive outflow rectification methods. Sludge. Technological scheme of wastewater rectification. Construction of aeration tank. Anaerobic wastewater rectification system. Methane fermentation, its phases.

### 5. Biotechnology in food and medicine industries.

Biotechnology in food industry. Industrial processes using enzymes: obtaining fructose syrup, L-amino acids, L-malic acid, 6-aminopenicillanic acid and other sweeteners.

Biotechnological processes in dairy industry. Lactic, propionic acid, butyric acid fermentation in preparation of dairy products. Technology of dairy products manufacture (yogurt, yogurt, acidophilus, godfathers, cheese, etc.). Biotechnological methods of whey processing, milk sugar obtaining.

Biotechnological processes in meat processing industry. The usage of start cultures and enzyme preparations to improve the quality of meat products. Processing of collagen and keratin-containing wastes of meat processing enterprises.

Production of medicamenta organotherapeutica. Raw materials for production of organic preparations. Classification of medicamenta therapeutica. Preparations of hormonal action: The preparations of pancreatic and thyroid, pituitary, adrenal, parathyroid glands. Preparations of enzymatic action: drugs and pancreatic al.

Biotechnological production bases of antibiotics. General information about antibiotics. Selection of producers of antibiotics. Fundamentals of antibiotics production technology.

Microbiological production of vitamins A, D, B2, B12: producers, special features of technology. Vaccines: classification of vaccines, technology for producing live vaccines and vaccines from killed pathogens cells, recombinant vaccine, antigens of the vaccine. Biotechnological bases of medical enzymes obtaining, diagnostic agents, hormones, and other bacterial and viral public immunization and curative drugs.