



Services

Valid from January 01, 2009



The services offered by our certified company are backed by more than 35 years of extensive experience.

We provide services to the pharmaceutical, medical devices, diagnostics and biotechnology industries, among others. All necessary laboratory facilities (BSL1, BSL2, S1) and permits as well as highly qualified employees are available to address your needs.

Our team includes virologists, microbiologists, biologists, physicians, veterinarians and bioengineers.

We are expert reviewers in the areas of microbiology and virology.

Development Methods (bioassays)
 Products (including CE certification and packaging)
 In vitro diagnostics
 Immunization (polyclonal antibodies)

Production Recombinant proteins in mammalian cells, etc.
 Viruses, bacteria and their antigens (BSL1, BSL2)
 Raw materials and active ingredients for pharmaceutical and diagnostics industries
 Antibodies (monoclonal, polyclonal)
 In vitro diagnostics

Testing Pharmaceutical (GxP)
 Medical devices, etc.
 Virology
 Microbiology
 Cytotoxicology
 Efficacy (veterinary vaccines)
 Physico-chemical tests
 Disinfectants (viruses, bacteria, fungi)

You will receive competent advice and reliable service directly from experienced scientists.

Your contacts:

Dr. Ingrid Rapp / Dr. Werner Dangel

Development

Our highly qualified team ensures that current research results and new technologies are incorporated in the development of new test and production procedures for our customers.

Years of collaboration with universities, research institutions and the BioRegion Ulm, as well as participation in federal and state funded projects ensure the necessary experience and technology exchange.



We can develop the following for you:

- Processes for production of recombinant proteins in mammalian cells or procaryotes
- Processes for production of baculovirus expressed proteins
- Test kits for medical diagnostics (including packaging and CE label)
- Test kit components (ELISA plates, slides, buffer systems, etc.)
- Detection methods for viral, bacterial and fungal infectious diseases
- Methods (bioassays) for monitoring production (IPC) and quality control
- Polyclonal antibodies through animal vaccination

Production

We produce on a commercial scale for diagnostics (DIN EN ISO 13485) and pharmaceutical manufacturers (GxP) according to specifications and the individual needs of our customers.

Our equipment:

- Fermentation units (scale up): Airlift, suspension or surface methods
- Numerous established cell lines (mammals, insects), viruses, bacteria and fungi
- Various concentration/purification procedures for protein recovery (downstream processing)
- GMP-Isolator
- Packaging and shipping



We produce:

- Viruses, bacteria and their antigens (BSL1, BSL2)
- Recombinant proteins on a commercial scale (cell culture)
- Polyclonal antibodies (own veterinary-supervised flock of sheep)
- Monoclonal antibodies on a commercial scale
- Raw materials and active ingredients for the pharmaceutical and diagnostics industries
- In vitro diagnostics (test kits) according to customer requirements

We test in accordance with international standards and guidelines (EN ISO, EP, USP, ASTM, etc.). We work with you to determine the optimal testing for you on the basis of your needs and resources. As an experienced diagnostics manufacturer and service provider, we know about the importance of cost-effectiveness, reliability, customer focus and high quality.

Our laboratory participates in various ring trials.



1. Virology testing

Manufacturing processes for pharmaceuticals or medical devices must be able to inactivate or deplete known and unknown viral contaminants. Early, targeted tests are also desirable in disinfectant manufacturing, starting in the development phase.

Process validation studies are performed in a validated downscale of the manufacturing process to determine the virus depletion rate or virus inactivation capacity. Our extensive experience in virology permits us to flexibly respond to customer requests and to apply our experience in downscaling of production processes and project implementation.

Furthermore we provide support in issues of safety to viral and infectious agents for purposes of legal regulations and normative requirements.

Our wide range of available test and reference viruses includes more than 50 different enveloped and non-enveloped viral strains, including animal and human pathogens with different physicochemical properties and resistances (see table 1, page 7)

Additional virus strains can be established at any time upon customer request. Various virus-sensitive cell lines are available for optimal virus culture.

1.1 Testing

Testing

Testing for viricidal effect

Validation of virus depletion in manufacturing processes

Examination for viral contamination

Application examples

Disinfectants, virostatics (also accompanying development)

Starting materials of animal or human origin, e.g. collagens, antibodies, heart valves, homografts, implantable medical devices

Raw material and end product testing in medical devices and pharmaceuticals, diagnostic antigens, hospital waste and sewage sludge samples

1.2 Techniques

Standardized functional assays and bioassays are performed in accordance with international and European standards and guidelines. The following techniques are available for virus detection:

Quantitative virus detection in cell culture (TCID50)
Plaque and plaque reduction tests
Molecular biology detection methods (PCR)
Immunological test systems (immunofluorescence, ELISA)
Haemagglutination tests
Haemadsorption tests

2. Microbiological tests

All microbiological tests are performed in accordance with international standards, norms and regulations (EP, USP, EN, and ISO). Our laboratory has a general handling licence for bacteria, viruses and fungi of biosafety level BSL-2. More than 60 bacteria and fungi have been established as reference and test strains.

Excerpt from our range of microbiological services:

Testing for sterility in the pharmaceutical and medical device industries, etc.: GMP-isolator, direct inoculation, membrane filtration method, validation of sterility tests

Bioburden determination in the pharmaceutical and medical device industries, etc.: Bioburden (validation) / product load, hygiene tests

Safety tests (raw materials, intermediate products and end products) and test procedures: According to customer requirements

Test for mycoplasmas according to EP 2.6.7

Microbial differentiation

Tests for adequate antimicrobial effectiveness

Validation of chemical and/or thermal disinfection methods and inactivation processes

Validation of sterilization processes: Validation of the sterilization of products with components of animal origin. Validation of gamma sterilization, steam sterilization, etc.

Examination of water samples (TrinkwV – drinking water ordinance)

3. Toxicological tests

Toxicity and compatibility tests in tissue cultures are a suitable alternative model for animal testing and

are used for basic testing of medical devices and for pharmacological screening tests. Cytotoxicity tests offer initial information about the biological compatibility of materials that were previously extracted with culture media or other suitable solvents. Cytotoxicity or growth inhibition is established either through measurement of the total protein content, which depends on the cell number, or through identification of the cells' metabolic activity.

Depending on the specific requirements, we perform standardized and quantifiable functional and bioassays in accordance with international and European standards.

4. Immunological tests

Immunological in vitro test systems with human leukocytes and methods for determining parameters of the innate and antigen-specific immune systems offer important information on immunosuppressive, anti-inflammatory and immunostimulating agents.

Phagocytic activity of leukocytes

Analysis through flow cytometry and FITC-labelled E. coli bacteria

Cytolytic activity of natural killer cells

For studies on spontaneous cytolytic activity, flow cytometry is used with PHK 26/PI-labelled K562 cells.

Cell proliferation - toxicity

The stimulating or suppressive effect of materials on peripheral blood mononuclear cells (PBMC) is tested using MTT assays and CFSE assays (based on flow cytometry)

Cytokines

Cytokines (with anti-inflammatory, immunostimulating or antiviral effect) are detected using enzyme immunoassays (ELISA)

In vitro inflammation model

Examination of surface modulation through expression of adhesion molecules (ICAMs, VCAMs, selectins) on human endothelial cells after the addition active substances. Analysis using flow cytometry and detection of inflammatory cytokines in ELISA.

Table1: List of established viruses, bacteria and fungi

Viruses
Adenovirus (bovine)
Adenovirus (human)
BVDV (bovine)
Calcivirus (feline)
Circovirus (porcine)
Coxsackievirus (human)
Cytomegalie virus (human)
Enzephalomyelitis virus (murine)
Epstein Barr virus (human)
FSME virus (human)
Hepatitis A virus
Hepatitis B virus (duck)
Herpes simplex virus (human)
Herpes virus (bovine)
Influenza virus (human)
Maedi visna virus (MVV)
Modified vaccinia virus (MVA)
Morbillivirus (human)
OPV bovis
Parainfluenza 3 (bovine)
Parainfluenza virus (human)
Parvovirus (bovine)
Parvovirus (porcine)
Polio virus (human)
PRRS virus
Reovirus type 3
Respiratory syncytial virus (human)
Rotavirus (bovine)
Rotavirus (human)
Rubella virus (human)
Rubulavirus (human)
Sarcoma virus (MuLV) (murine)
Sindbis virus
Sv 40
Vacciniavirus (strain Elstree)
Varizella zoster virus (human)
Vesikular stomatitis virus (VSV)

Bacteria
Acholeplasma laidlawii
Bacillus atrophaeus
Bacillus cereus
Bacillus pumilus
Bacillus stearothermophilus
Bacillus subtilis
Bordetella pertussis
Brevundimonas diminuta
Clostridium sporogenes
Enterobacter aerogenes
Enterobacter intermedius
Enterococcus faecalis

Enterococcus faecium
Enterococcus hirae
Escherichia coli
Haemophilus actinomycetem comitans
Klebsiella pneumoniae
Lawsonia intracellularis
Legionella pneumophila subsp. Pneumophila 7531
Listeria monocytogenes
Micrococcus luteus
MRSA
Mycobacterium avium
Mycobacterium terrae
Mycobacterium thermoresistibile
Mycoplasma hyorhinis
Mycoplasma orale
Mycoplasma pneumoniae
Porphyromonas gingivalis
Proteus mirabilis
Pseudomonas aeruginosa
Salmonella montevideo
Salmonella paratyphi
Salmonella typhi
Serratia marcescens
Staphylococcus haemolyticus
Staphylococcus simulans
Staphylococcus epidermis
Staphylococcus aureus
Stenotrophomonas maltophilia
Streptococcus sp. (viridans)
Streptococcus mutans
Streptococcus pyogenes
Yersinia enterocolitica

Fungi
Aspergillus fumigatus
Aspergillus niger
Candida albicans
Fusarium solani
Saccharomyces cerevisiae