Pharma Chemicals

Biocatalysis

BioCAT Platforms

Enzyme Platforms	Product Classes
Aldolases	Alcohols, Diols, Amino acohols
Proteases	Peptides, Amines, Carboxyesters
Lipases and Esterases	Alcohols, Esters, Carboxylic acids
Ammonia lyases	Amino acids
Hydantoinases, Carbamoylases, Racemases	Amino acids
Amidases	Amino acids
Acylases	Amino acids, N-Acetyl-Amino acids
Hydroxynitrile lyases	Cyanohydrins
Omega-Transaminases	Amines
Oxidases	Alcohols, Aldehydes, Carboxylic acids
Dehydrogenases (alcohol & amino acid)	Alcohols and Amino acids
Nitrilases	Carboxylic acids, Nitriles
Nitrile hydratases	Amides, Nitriles
Monooxygenases (P450, Baeyer-Villiger)	Alcohols, Sulfoxides
Epoxide hydrolases	Epoxides, Diols
Haloalcohol dehalogenases	Epoxides, Diols

Used in tons scale production
Used in lab pilot scale

DSM offers recognized expertise in the use of enzymatic processes for complex chemical synthesis. As one of the leading enzyme manufacturers worldwide, we also have an extensive background in food-grade and cGMP enzyme production technology, which enables us to identify solutions to demanding production requirements.

Our track record for innovation is unrivalled—with the introduction of at least one new enzymatic process per year on average. This is reflected in more than 30 processes during our substantial history in applied biocatalysis.

We rapidly identify the right biocatalyst from our BioCat Platforms—comprising a continually increasing number of off-the-shelf enzymes—and have access to wide biodiversity, mutant libraries, and a variety of efficient production organisms. Our experience ensures rapid process optimization and scale up with rapid reaction optimization, and supports process development and full-scale cGMP implementation.

We also support regulatory criteria concerning the safe use of enzymes and full-scale cGMP implementation. This is exemplified by the development of PharmaPLE®—a pharmaceutical form of the useful enzyme pig liver esterase, which has been proven for various pharmaceutical intermediates already at manufacturing scale. In addition, we apply a huge spectrum of different enzymes as shown in the below table. Most recently, we introduced a new omega-transaminase and ammonia lyase process for ton scale production of a chiral amine and amino acid intermediate.

DSM
BRIGHT SCIENCE. BRIGHTER LIVING.

Pharma Chemicals

Applications for Biocatalysis

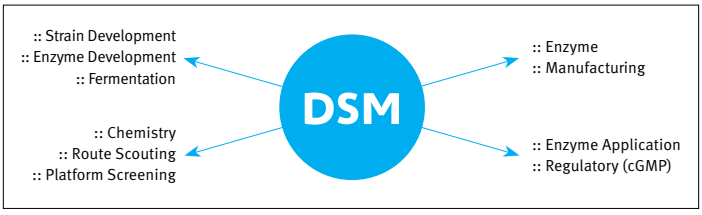
A challenge particular to pharmaceutical manufacturing is increasingly complex molecules demanding more steps in the chemical synthesis. According to recent analysis, there are typically eight steps for synthesis of an API. The high erosion rate of drug candidates doesn't justify extensive route scouting and early-phase process development. Focus instead lies in speed of delivery rather than cost efficiencies.

Biocatalysis was previously a niche technology due to a limited number of easily accessible biocatalysts, lengthy development timelines, and high costs. During the last decade, breakthroughs in molecular biology, analytics, bioinformatics, and gene synthesis have led to large databases of efficient biocatalysts and genes. Enzymes are readily available and can be rapidly produced at DSM on any scale.

DSM's PluGbug® expression system uses tools that drastically reduce timelines in the scale up of enzyme production from years to weeks. In addition, our efforts in providing the most advanced enzyme screening services have resulted in rapid growth of our enzyme collection, increasing from several hundred to more than 2,000 enzymes in 10 years. Easier access to more robust and versatile biocatalysts, combined with cost pressures, are driving increasing opportunities for biocatalysis across all phases of drug development.

DSM is a leader in this technology development, as one of the few enzyme service providers with strong chemistry expertise and contract manufacturing capabilities to offer flexible and open partnering with access to a broad enzyme toolbox and interdisciplinary route scouting expertise.

The main benefit in biocatalysis still lies in developing second-generation processes for late clinical phases or launched APIs. However, improved access to enzymes enabling chiral transformations such as hydroxylations or other chemo and regioselective modifications might also offer new opportunities for biocatalysis in early phase of development—enabling reactions that are extremely difficult or impossible by classical means.



Combined strengths in biotechnology and chemistry with experience in large scale cGMP manufacturing makes DSM unique in biocatalysis

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