

GMM DERIVED ENZYMES, ENZYME SAFETY & REGULATIONS

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Nutrition & Biosciences



Our Journey to Three: Creating World Leading Companies

2017

We brought together the complementary, innovative portfolios and pipelines of Dow and DuPont



2019

With the intent to create three strong, independent companies

April



Materials
Science

June



Agriculture

June



Specialty Products

Welcome to a new DuPont

Specialized solutions

Essential innovations from highly engineered products and naturally sourced ingredients to shape industries and everyday life

2019



Transforming Everyday Lives in 70+ countries



Nutrition & Biosciences Touches People's Lives Everyday

140 billion



Scoops of ice-cream sold containing DuPont ingredients

1 in 3



Pharmaceutical tablets sold globally with DuPont ingredients

60%



DuPont enzyme technology used in laundry wash loads across the globe

4 billion



Times per year that DuPont alginates bring acid reflux relief to consumers

11.7 million



Car equivalent CO₂ removed through ethanol in gasoline in 2018. DuPont is a leader in providing enzyme and yeast technologies for ethanol

1 in 3



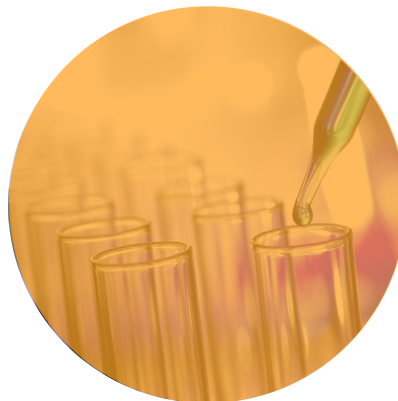
Probiotic supplements sold globally with DuPont probiotics

Serving Customers Through Three Strong Platforms



Food & Beverage

- › Functional Solutions
- › Emulsifiers & Sweeteners
- › Protein Solutions



Health & Bioscience

- › Probiotics, HMO, Fibers
- › Cultures, Food Enzymes, Food Protection
- › Animal Nutrition
- › Grain Processing
- › Household & Personal Care
- › Microbial Control



Pharma Solutions

- › Pharma Excipients
- › Global Specialty Solutions
- › Nitrocellulose

Our Core Values



**Safety &
health**



**Respect for
people**



**Highest ethical
behavior**



**Protect the
planet**

Nutrition & Biosciences

DUPONT

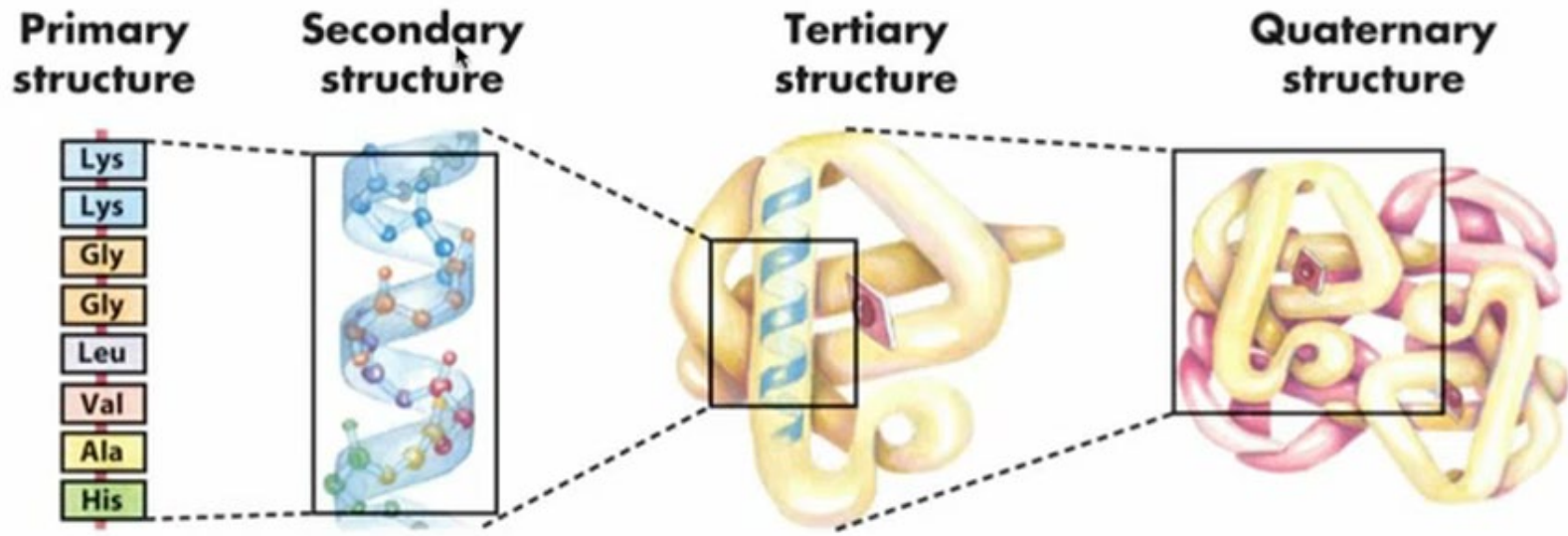
Nutrition & Biosciences

DUPONT

ENZYMES

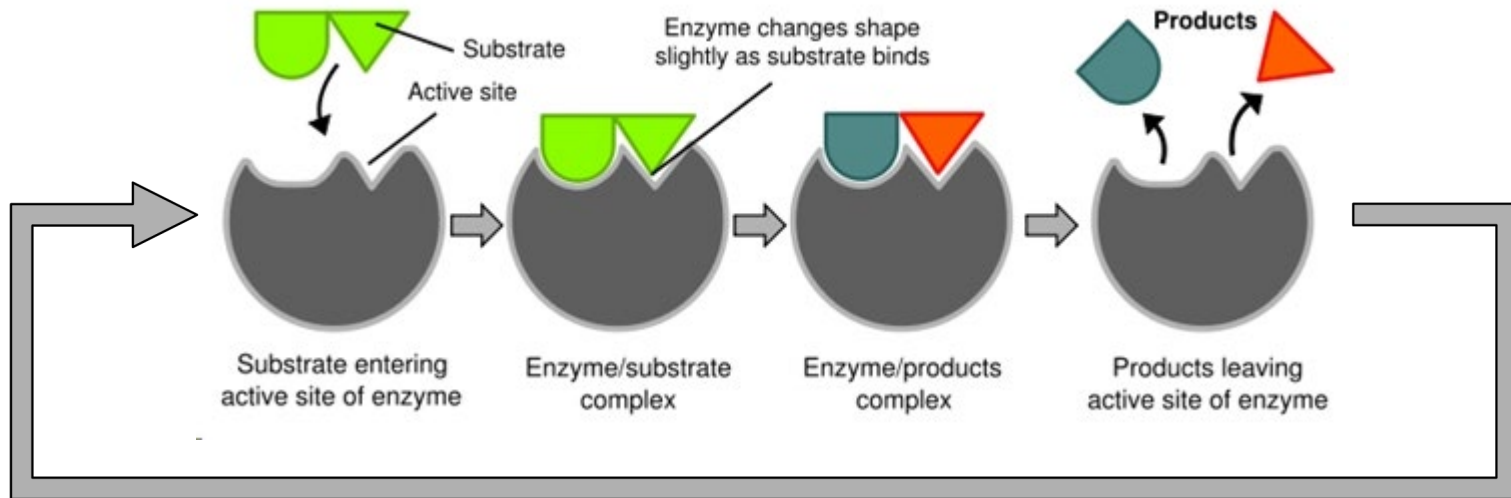
Enzymes Are Proteins

- Chains of amino-acids (20)
- Folded into a 3-dimensional structure
- Produced by plant, animals and microorganisms (naturally occurring)



Enzymes Are Natural Catalysts

- They speed up chemical reactions, lowering the energetic threshold
- They are specific (substrate + reaction)
- Required in very small amounts as they are not consumed during the reaction



Classification according to reaction catalyzed by the enzyme:

- International Union of Biochemistry and Molecular Biology

Enzymes Have Long History of Safe Use



How are enzymes used?



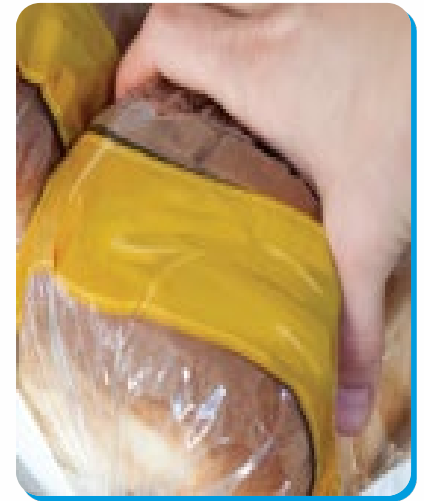
Animal Nutrition



Home & Personal Care



Grain Processing



Food Processing

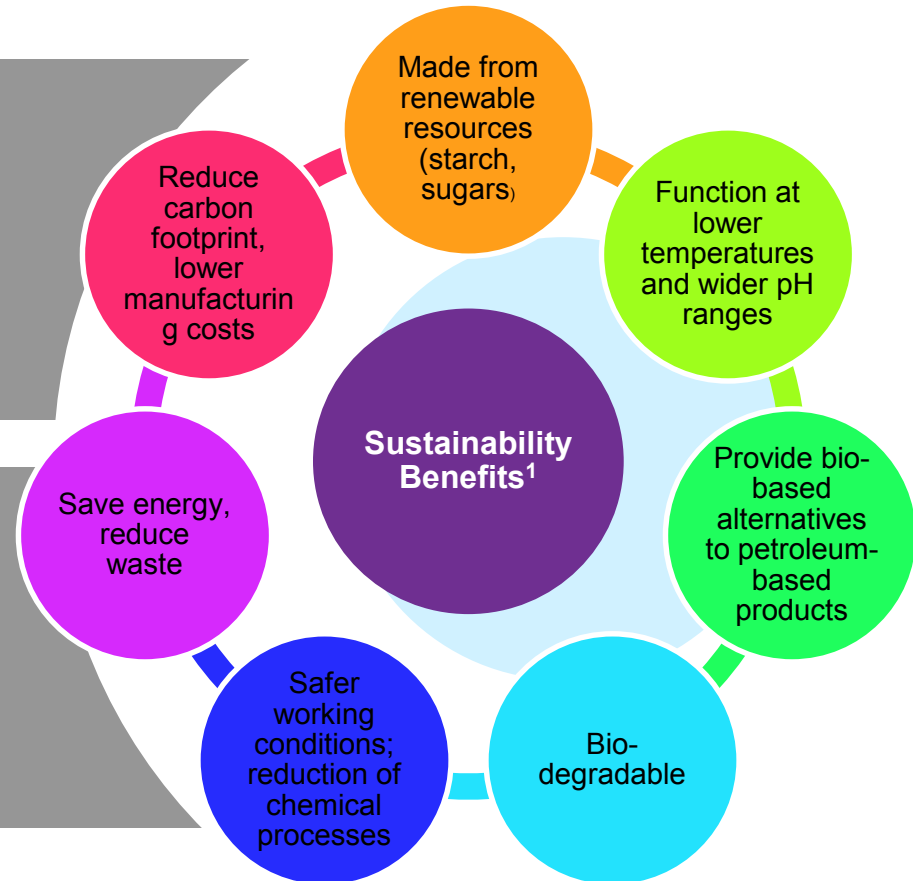
Sustainability benefits of enzymes



Enzymes often replace less efficient chemicals and can save energy, reduce waste, and more efficiently convert raw materials into desired end products



Though the amount of enzymes added to accomplish a reaction is relatively small, the sustainability benefits are significant



DEVELOPMENT & SCALE UP



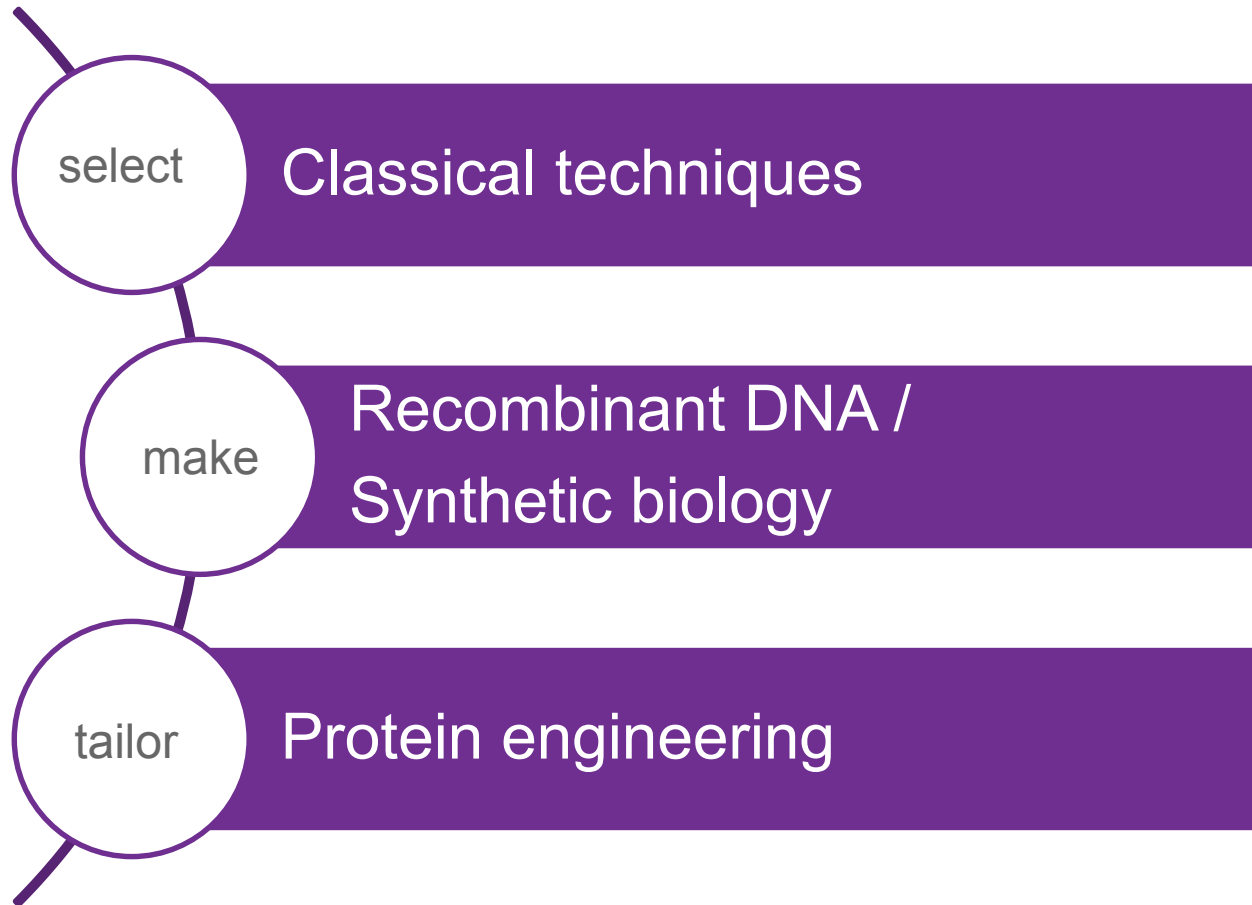
Why Microbial Enzymes?

Sourced from bacteria, fungi and yeast

Preferred over the enzymes sourced from plants and animals because

- ✓ Can tailor the enzyme to the application
 - ✓ More controlled process
 - ✓ More consistent in quality
 - ✓ More cost-effective to produce
 - ✓ **Safer**
- Well-established published safety evaluation procedures for enzymes produced with modern biotechnology, which take into account the enzyme, the production organism, the manufacture process, and safety studies:
 - Pariza & Cook (2010); Sewalt et al. (2016)

Approaches to the Development of Enzyme Products



How Enzymes are made



FROM LAB TO CONSUMER PRODUCT:

Scientists engineer the metabolic pathways of micro-organisms to produce enzymes, proteins, and other bio-molecules at industrial scale

Commercial enzymes are produced from the fermentation of specially selected nonpathogenic, nontoxigenic strains of microorganisms

Enzyme products are formulated into products using a variety of physical forms: Liquids, slurries, granules, and powders

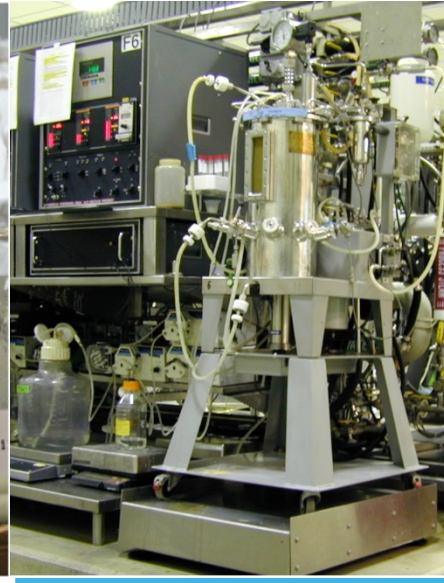
Fermentation Processes Are Built from the Ground Up



5 mL



250 mL

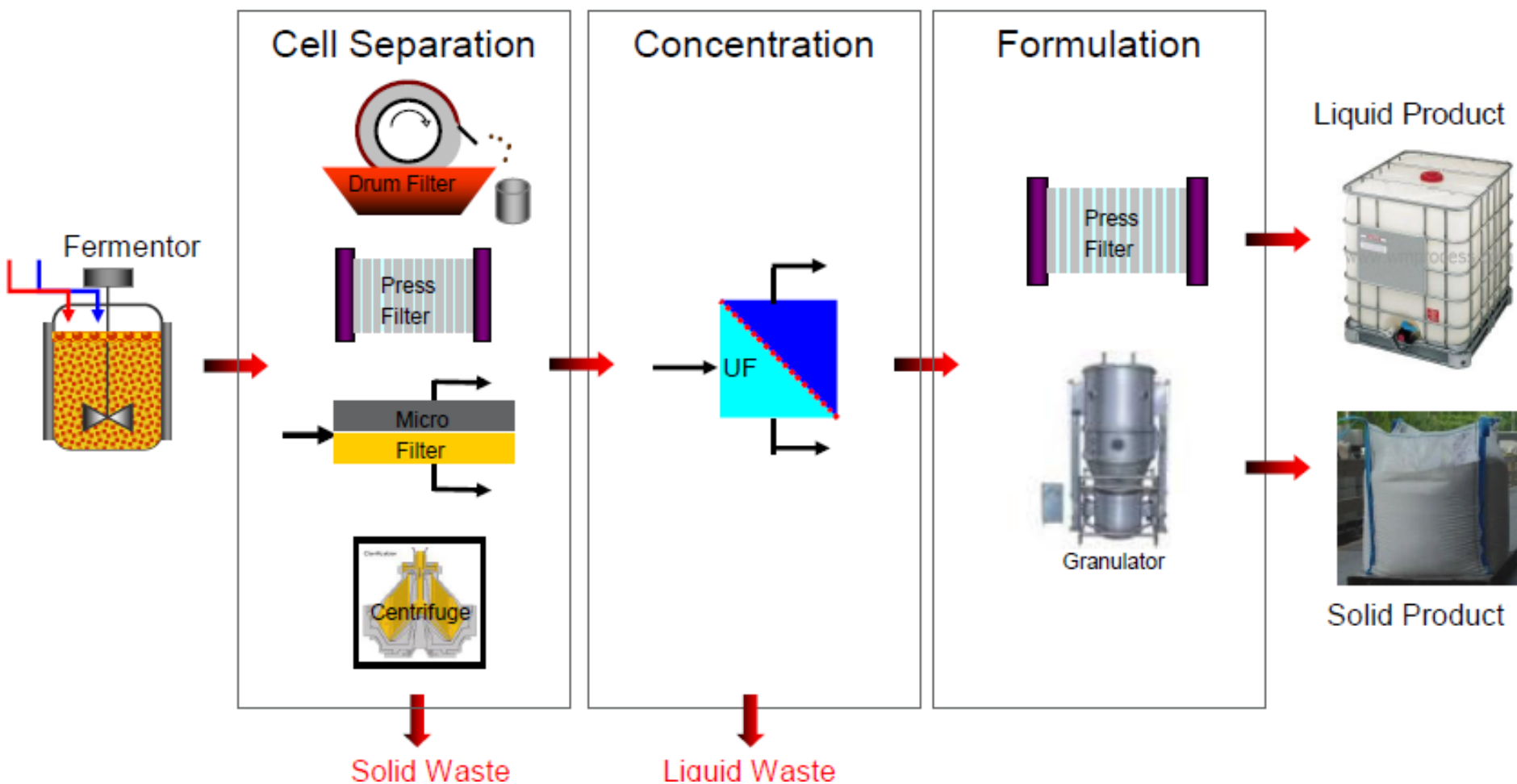


15 L



> 100,000 L

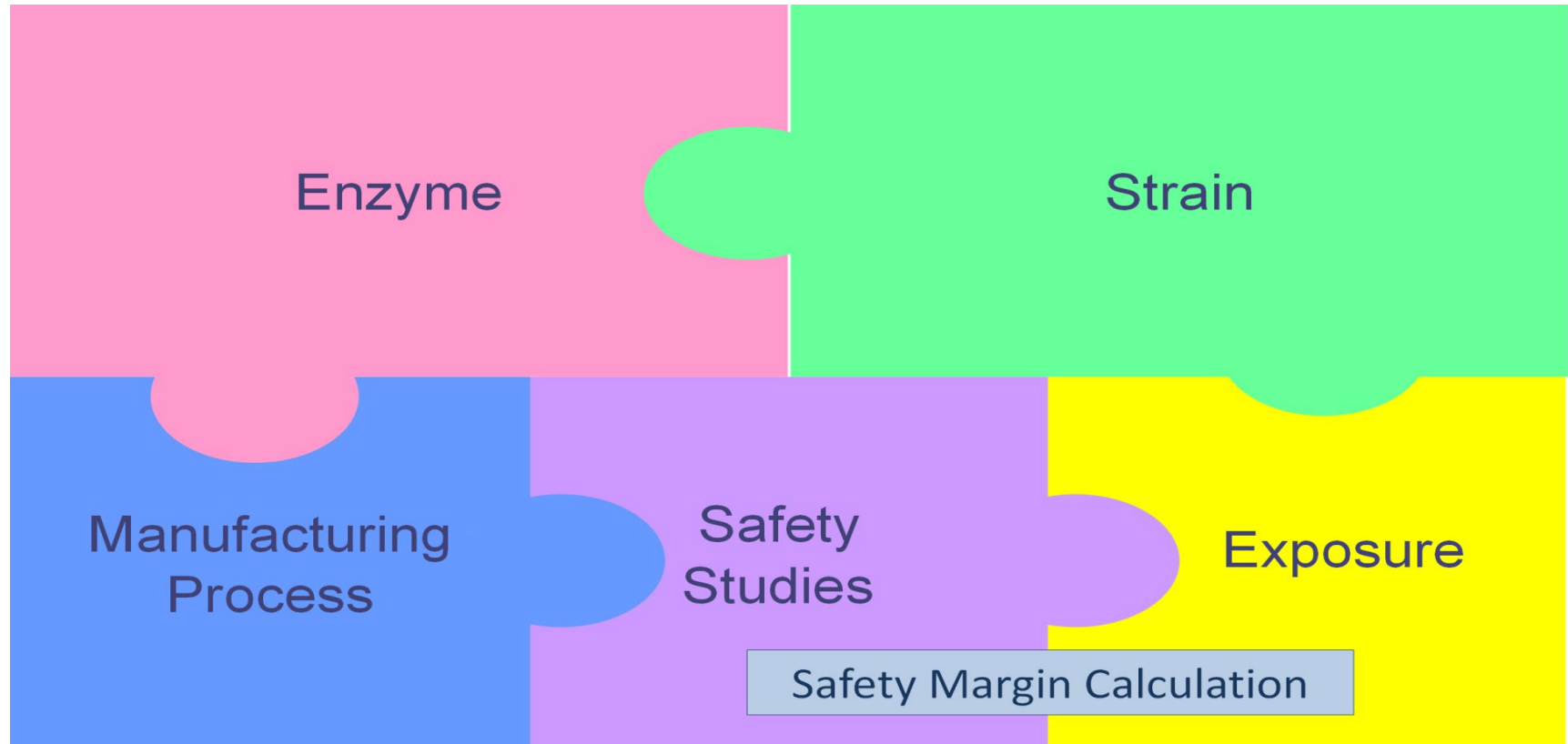
Typical Industrial Enzyme Production Process



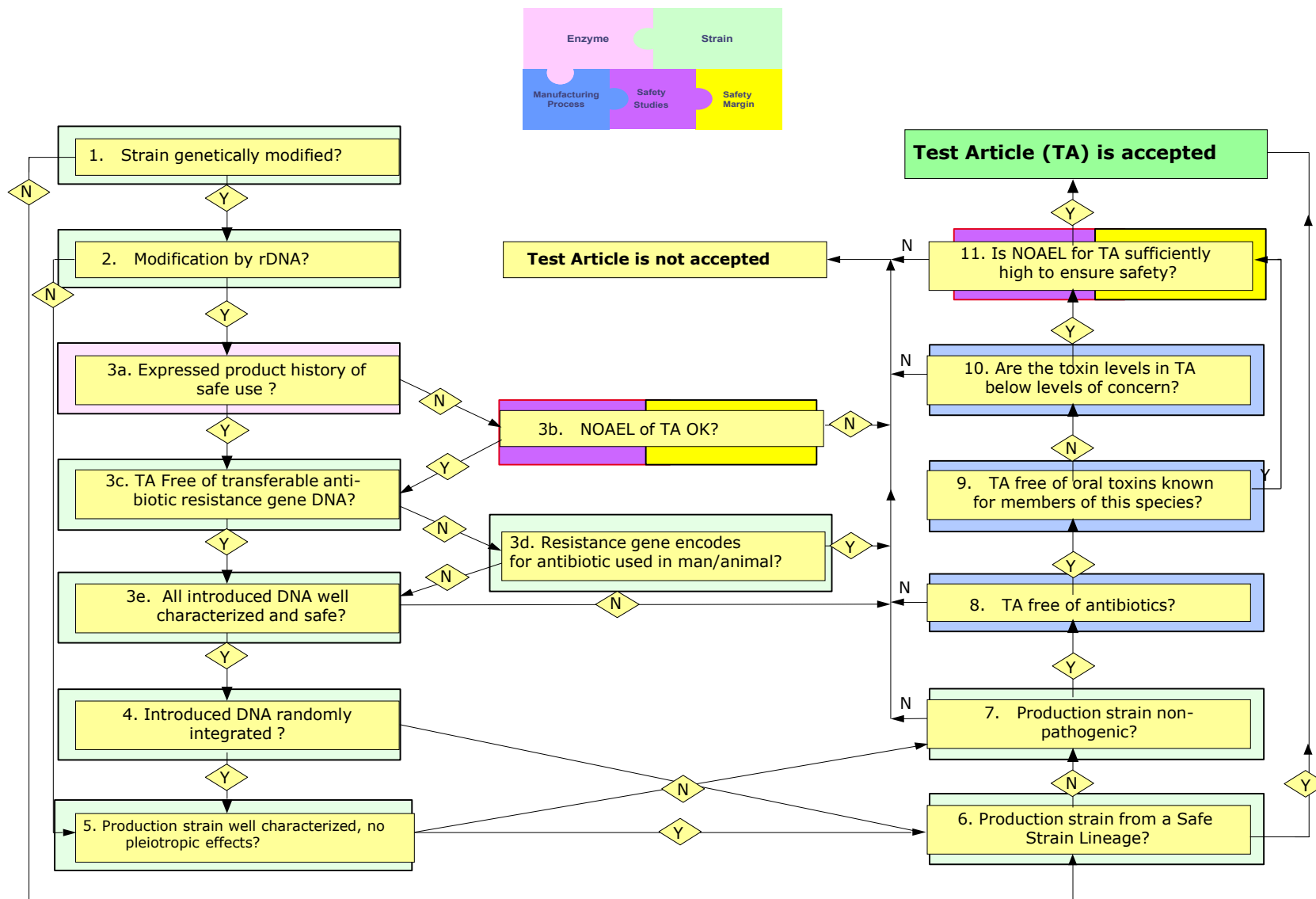
ENZYME SAFETY

Safety Evaluation of Food Enzymes

5 Essential Elements:



Pariza & Johnson (2001) Decision Tree





General Enzyme Safety

Enzymes are ‘Intrinsically safe’ proteins (Olempska-Beer *et al.*, 2006)

- Can be categorized as “practically non-toxic”... based on 40+ years of testing, use in commerce, and an in-depth knowledge of their properties
- Lack of oral toxicity, not reproductive or developmental toxins

Lack of Genotoxicity

- Enzymes are not mutagenic, and not clastogenic
- Supported by plethora of data, e.g. Pariza & Johnson (2001) reported over 100 Ames assays and over 60 Chromosomal Aberration studies, all testing negative.

Enzymes are used at very low levels

- Any contaminants, if present, would be at ‘*de minimis*’ levels.

Industry Handling safety

- As with any protein, enzymes, when inhaled, have the potential to elicit an allergic response in atopic individuals
- Proteases can irritate skin and mucous membranes

REGULATORY PROVISIONS

Regulatory provisions

- **AUSTRALIA AND NEW ZEALAND:** Positive List (updated 23rd August 2018):
<https://www.legislation.gov.au/Details/F2017C01002>
- **BRAZIL:** List of Permitted Enzymes for Food Use (November 2014) : Issued by Ministry of Health (Brazilian positive list for food enzymes)
- **DENMARK:** Issues Health Certificates to authenticate approvals by authority
- **JECFA:** <http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/>
- **SINGAPORE:** List of Permitted Enzymes for Food Use (March 2017) : Issued by Singapore Food Agency (SFA).

<https://sso.agc.gov.sg/SL-Supp/S152-2017/Published/20170331?DocDate=20170331>

Regulatory provisions

- **USA:** <https://www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices>
- **INDIA:**
 - Processing Aid
 - GMM absence
 - Safe Usage History



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