

Formulation Technologies and Commercial Translation of Biological Agricultural Products: An Integrated Framework from Product Design to Market Readiness

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Abstract

Biological agricultural products are moving from niche inputs toward integrated platforms for crop protection, nutrition, and stress management, yet their commercial success remains strongly formulation-dependent. This review critically integrates formulation science, process scale-up, surfactant and inert chemistry, quality-by-design principles, analytical control, regulatory strategy, registration support, and techno-economic considerations across biopesticides for weed, insect, and plant-disease management, biofertilizers, and biostimulants. Particular attention is given to emulsion concentrates (EC), oil dispersions (OD), suspension concentrates (SC), wettable powders (WP), and water-dispersible granules (WG), while emphasizing that viable microbial active ingredients impose constraints fundamentally different from those of botanical extracts, fermentation metabolites, and other biochemical actives. The review links interfacial chemistry, wetting, dispersion, rheology, water activity, oxygen and moisture exposure, carrier selection, preservative strategy, and packaging to storage stability and field delivery. Scale-up is treated as a product-development problem rather than simple volumetric enlargement, with emphasis on mixing regime, shear history, heat transfer, contamination control, drying stress, particle-size distribution, viable-count or active-content recovery, and batch-to-batch reproducibility. Regulatory pathways are compared conceptually for microbial and biochemical pesticides, fertilizers, and biostimulants, and a stage-gated framework is proposed to connect formulation composition, manufacturing description, specifications, stability, efficacy, safety, analytical methods, and commercial decision-making. Cost-of-goods considerations are integrated with formulation selection to show how fermentation yield, downstream recovery, drying, packaging, cold-chain avoidance, and field application rate influence commercial feasibility. The resulting formulation-by-biological-class decision framework provides a practical basis for developing robust, scalable, analytically defensible, and registration-ready biological agricultural products.

Keywords: biopesticide; bioherbicide; bioinsecticide; biofungicide; biofertilizer; biostimulant; emulsion concentrate; oil dispersion; suspension concentrate; wettable powder; water-dispersible granule; surfactant; scale-up; registration; quality control

1. Introduction

Biological inputs now span microbial pesticides, botanical and fermentation-derived biochemical pesticides, microbial and non-microbial biostimulants, and biofertilizers. Recent reviews emphasize that successful biological products must be designed around the intended target, use pattern, production constraints, formulation, safety and commercialization pathway rather than biological efficacy alone (Cai and Dimopoulos 2025; Glare et al. 2026). Their commercial value depends not only on biological activity but on conversion of an active ingredient into a product that can be manufactured reproducibly, stored for a practical period, transported through variable climates, diluted or applied reliably, and supported by defensible analytical and regulatory data. Formulation therefore links discovery with commercialization; fungal bioherbicides and metabolite-based products illustrate this dependence

particularly clearly (Singh and Pandey 2019b, 2022b). For microbial pesticides, the formulation must preserve viability, infectivity or metabolically relevant activity; for cell-free metabolites and botanical actives, it must protect chemical integrity, solubility and bioavailability; for biofertilizers and microbial biostimulants, it must maintain viable populations and functional traits until use (Burgess 1998; Jones and Burgess 1998; Bashan et al. 2014; Vassilev et al. 2020).

Regulatory classification is equally important because the same organism or metabolite can face different data expectations depending on intended claims. In the United States, microbial and biochemical pesticides are regulated as biopesticides with specific data requirements, whereas the European Union applies microorganism-specific principles for plant-protection products. In India, biostimulants are regulated under the Fertilizer (Control) Order framework, while pesticidal products are handled

through the pesticide regulatory system. Consequently, formulation development should begin with a target product profile that defines biological identity, claim, use pattern, dose, shelf life, package, application equipment, target markets and registration pathway (U.S. EPA 2026; European Commission 2022a, 2022b; Government of India 2025).

This review critically evaluates five widely used formulation platforms—EC, OD, SC, WP, and WG—for biological products used in weed, insect, and plant-disease management and in plant nutrition and stimulation. Its distinctive contribution is to treat formulation selection, scale-up, quality attributes, analytical control, regulatory evidence, and cost per treated hectare as interdependent development decisions rather than isolated technical activities. The resulting framework is intended to support early go/no-go decisions and reduce late-stage reformulation, registration delays, and commercially weak product designs.

2. Biological Active Ingredients and Formulation Requirements

2.1 Microbial pesticides for weeds, insects and plant diseases

Microbial herbicides, insecticides and fungicides may contain fungal conidia, blastospores, bacterial cells or spores, viruses, protozoa, or mixtures of viable propagules and biologically active metabolites. Their formulation requirements are governed by desiccation tolerance, oxygen demand, membrane sensitivity, germination behavior, compatibility with oils and surfactants, and sensitivity to temperature, ultraviolet radiation and water activity. Fungal conidia are often better suited to dry powders or oil-based systems than fragile submerged propagules, while bacterial endospores commonly tolerate drying and solid carriers better than vegetative cells (Burgess 1998; Jackson et al. 2010; Mascarin and Jaronski 2016).

2.2 Biochemical, botanical and cell-free products

Botanical extracts, microbial metabolites, enzymes, semiochemicals and cell-free fermentation products behave more like chemical actives than living cells, although they may be chemically complex and less stable than conventional pesticides. Solubility, partition coefficient, pKa, hydrolysis, oxidation, photolysis and volatility influence whether an EC, OD, SC, encapsulated system or dry formulation is technically appropriate. Natural-product

mixtures also require marker-based analytical specifications because a single nominal active may not fully describe biological potency (Copping and Menn 2000; Isman 2006; Dayan et al. 2009). Fungal metabolites and cell-free fungal broths have been proposed as practical routes to natural herbicides, which makes stability, standardization and marker-based specification central to their formulation (Singh and Pandey 2019a, 2020, 2022b, 2025a, 2025d).

2.3 Biofertilizers and Biostimulants

Biofertilizers based on *Rhizobium*, *Azotobacter*, *Azospirillum*, phosphate-solubilizing microorganisms, potassium-mobilizing microorganisms, cyanobacteria and arbuscular mycorrhizal fungi require preservation of viable and functional inoculum. Biostimulants are broader and may include microorganisms, seaweed extracts, humic substances, protein hydrolysates and other materials that stimulate plant processes rather than directly control pests. Carrier selection, moisture, pH, osmotic stress and contaminant exclusion are central to microbial inoculants, whereas non-microbial biostimulants require chemical stability, compositional consistency and appropriate marker methods (Bashan et al. 2014; du Jardin 2015; Roupael and Colla 2020).

3. Core Formulation Technologies

The conventional formulation codes EC, OD, SC, WP and WG are useful engineering categories, but their direct transfer to biological products must be evidence-based. Contemporary formulation reviews additionally highlight encapsulation, controlled-release and nano-enabled systems, while stressing that added complexity must be justified by measurable gains in stability, delivery or field performance (Gundreddy et al. 2024; Senthil-Nathan et al. 2026). A living microorganism should not be placed into a solvent or surfactant environment merely because that formulation is standard for a synthetic active. Compatibility testing must measure not only physical stability but also viability, germination, infectivity, enzyme activity or other product-specific potency endpoints.

Selection of an appropriate formulation platform depends primarily on the physicochemical nature of the active ingredient, sensitivity to water and processing conditions, solubility, requirement for maintaining microbial viability, and intended application route. A practical decision framework for selecting among EC, OD, SC, WP and WG systems is presented in Fig. 1 and Table 1.

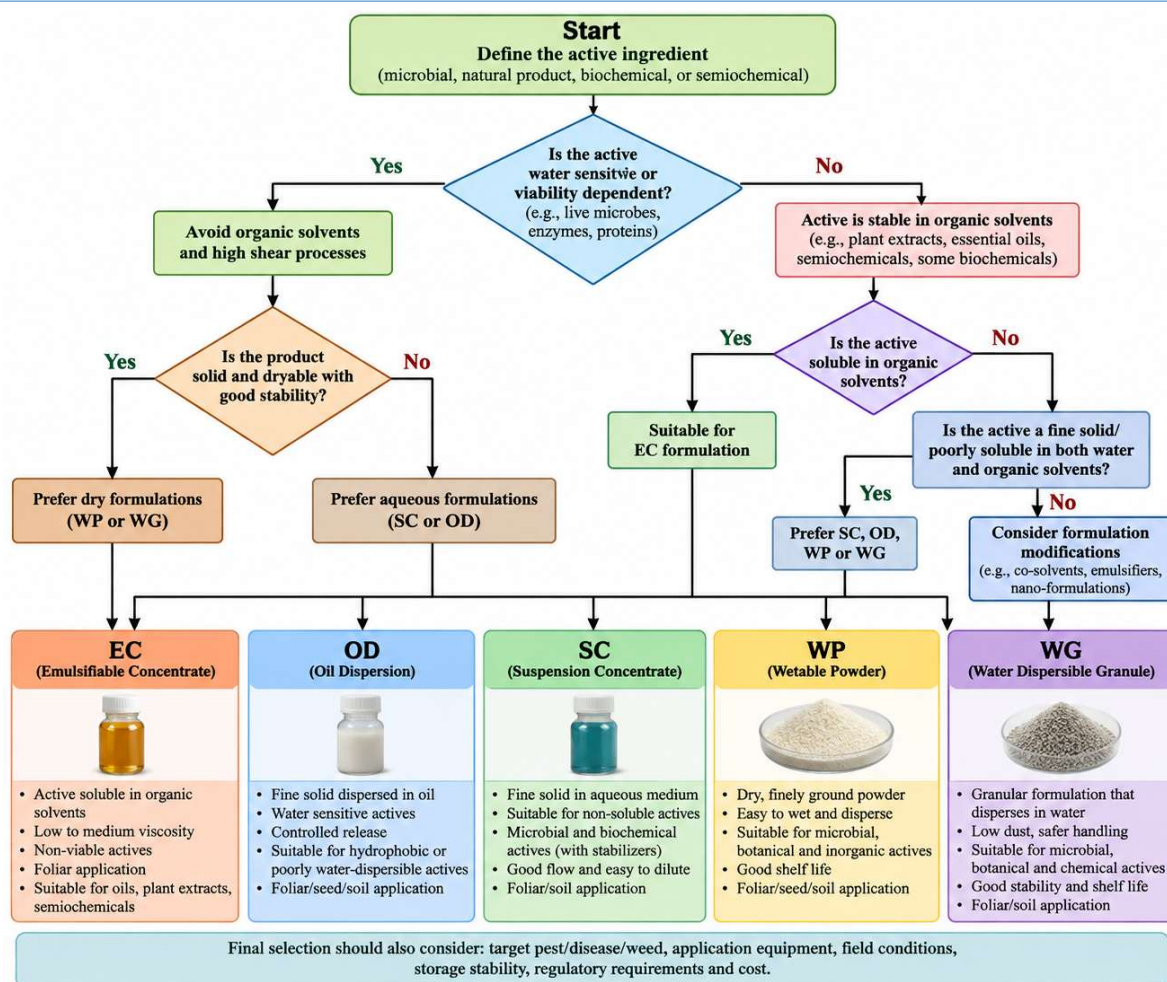


Fig. 1. Decision framework for selection of EC, OD, SC, WP and WG formulation systems for biological agricultural products based on active-ingredient type, water sensitivity, solubility, viability requirements and intended application route.

Table 1. Comparative suitability of major formulation platforms for biological agricultural products

System	Physical basis	Typical strengths	Main risks	Microbial pesticides	Biochemical/botanical actives	Biofertilizer/biostimulant fit
EC	Active dissolved in organic/oily phase with emulsifier	Simple manufacture; rapid dilution; strong spreading	Solvent toxicity, flammability, cell incompatibility, crystallization	Usually poor for live cells; possible for non-living metabolites	Good when active is oil-soluble and solvent-stable	Mainly non-microbial biostimulants
OD	Solid active dispersed in oil	Rainfastness, adhesion, reduced water exposure	Sedimentation, viscosity drift, oil/surfactant toxicity	Often promising for fungal conidia/spores after compatibility testing	Good for poorly water-soluble solids	Possible for stress-tolerant microbes; uncommon for classic inoculants

System	Physical basis	Typical strengths	Main risks	Microbial pesticides	Biochemical/ botanical actives	Biofertilizer/ biostimulant fit
SC	Fine solid active dispersed in water	Easy handling; no dust; good metering	Hydrolysis, microbial contamination, sedimentation, viability loss	Suitable only when aqueous stability is demonstrated	Strong option for insoluble stable actives	Useful for some liquid microbial inoculants with controlled water activity
WP	Dry powder dispersible in water	Low water activity; simple equipment; good stability	Dust, poor wetting, caking, operator exposure	Widely applicable to spores and dry biomass	Suitable for solid actives	Common carrier-based inoculant concept
WG	Granules disintegrating/dispersing in water	Low dust; better handling; accurate dosing	Granulation/drying stress; disintegration failure	Good if granulation preserves viability	Good for stable solids	Promising for robust microbes and dry biostimulants

3.1 Emulsion concentrate (EC)

An EC is conventionally a homogeneous liquid in which the active ingredient is dissolved in a water-immiscible or partly miscible solvent system and emulsifies after dilution. EC development begins with solvent screening, active solubility, low-temperature crystallization, emulsion quality in waters of different hardness, and emulsifier hydrophilic–lipophilic balance. For biological products, EC is primarily relevant to botanical oils, lipophilic metabolites and other non-living biochemical actives. Many conventional solvents and concentrated surfactants are unsuitable for viable microorganisms because they disrupt membranes or extract cellular lipids. Where an EC-like product is considered for a biological metabolite, solvent toxicology, flash point, packaging compatibility and inert regulatory status must be included in the target product profile.

3.2 Oil dispersion (OD)

OD formulations contain fine solid particles dispersed in an oil phase and stabilized by dispersants, wetting agents, rheology modifiers and anti-settling agents. The low-water environment can be advantageous for fungal conidia by limiting premature germination and hydrolytic deterioration, while the oil phase can improve adhesion and spreading on hydrophobic plant or insect surfaces. However, oils differ substantially in oxidation stability, viscosity and biological compatibility. Vegetable oils, methylated seed oils, mineral oils and synthetic esters should therefore be screened with the complete surfactant

package rather than individually. Accelerated centrifugation, sedimentation, redispersibility, viscosity and viable-count retention are useful development endpoints (Burgess 1998; Mascarín and Jaronski 2016).

3.3 Suspension concentrate (SC)

An SC is a concentrated dispersion of finely divided insoluble active particles in a continuous liquid phase, commonly water. Physical stability depends on particle-size distribution, density difference, continuous-phase viscosity, surface charge and steric stabilization. Milling can improve suspension behavior but can also generate heat and shear that damage biological structures. For microbial SC products, formulation water must be treated as an active design variable: water activity, osmotic potential, pH, dissolved oxygen, preservatives and nutrient carryover can determine whether cells remain stable or begin unwanted growth. For biochemical solids, the central challenge is prevention of crystal growth, hard settling and chemical degradation.

3.4 Wettable powder (WP)

WP formulations combine a dry active with carriers, wetting agents and dispersants so that the product rapidly wets and forms a suspension after dilution. They remain attractive for microbial spores because low water activity can support shelf life and the manufacturing process can be comparatively simple. Carrier candidates include clays, silica, starches, mineral fillers and selected organic

materials, but each can affect moisture sorption, pH, viability and dust generation. Fine powders increase surface area and dispersion but also increase inhalable dust and caking risk. Moisture-barrier packaging is therefore part of the formulation system rather than an afterthought.

3.5 Water-dispersible granule (WG)

WG products are free-flowing granules that disintegrate and disperse in water. Compared with WP, they reduce dust and improve handling. Manufacturing routes include wet granulation, extrusion, fluid-bed granulation and agglomeration. The main biological challenge is that granulation and drying can expose microorganisms or sensitive metabolites to water, heat, pressure and shear. Protectants such as sugars, proteins, polyols and polymers may improve survival, but they can alter disintegration and storage hygroscopicity. A successful WG therefore balances granule strength during transport with rapid disintegration in the spray tank.

4. Surfactant Chemistry and Interfacial Design

Surfactants determine wetting, emulsification, dispersion, spreading, adhesion and sometimes biological

uptake. Their selection should be based on molecular structure and system behavior rather than trade name alone. Nonionic surfactants are widely used because they are less sensitive to water hardness and electrolyte concentration than many ionic surfactants. Anionic surfactants can provide strong wetting and electrostatic stabilization, while polymeric dispersants provide steric barriers against aggregation. Cationic surfactants are often antimicrobial and therefore require particular caution in living microbial products.

Hydrophilic–lipophilic balance provides a useful first approximation for emulsifier selection, but final optimization requires empirical phase behavior and dilution testing. Critical micelle concentration, cloud point, dynamic surface tension, contact angle and interfacial rheology can be more informative than static surface tension alone. For foliar biologicals, the ideal adjuvant improves deposition without destroying spores, cells, viral occlusion bodies, enzymes or metabolite activity. Surfactant concentration should therefore be evaluated as a dose-response variable for both physical performance and biological potency.

Table 2. Functional classes of formulation auxiliaries and key compatibility questions

Auxiliary	Primary function	Examples/classes	Key analytical test	Biological compatibility concern
Wetting agent	Rapid displacement of air and wetting of powder/leaf	Nonionic ethoxylates, sulfosuccinates, alkyl polyglucosides	Wetting time, contact angle, surface tension	Membrane injury; germination inhibition
Dispersant	Prevent flocculation/agglomeration	Lignosulfonates, polyacrylates, naphthalene sulfonate condensates, polymeric dispersants	Suspensibility, zeta potential, particle-size drift	Osmotic/electrolyte stress
Emulsifier	Stabilize oil-water interface	Nonionic/anionic blends, sorbitan esters, polysorbates	Emulsion stability, droplet size	Solubilization of membrane lipids
Rheology modifier	Reduce settling and control flow	Xanthan, cellulose derivatives, clays, fumed silica	Viscosity/rheology, redispersibility	Entrapment, oxygen-transfer changes
Humectant/protectant	Reduce drying injury and improve persistence	Glycerol, sorbitol, trehalose, skim milk/proteins	Water activity, viability after drying	May support contaminant growth
Antifoam	Control foam in manufacture/application	Silicone or non-silicone antifoams	Foam persistence	Potential coating/interfacial effects
Preservative	Control contaminants in non-sterile aqueous products	Product-specific permitted preservatives	Microbial limits, challenge test	May kill intended microorganism

5. Inert Ingredient and Carrier Compatibility

Inert ingredients are functionally active components of a formulation even when they have no pesticidal claim. A robust compatibility program evaluates immediate toxicity, chronic storage effects and performance after dilution. Screening should include pH, conductivity, osmolality, water activity, peroxide value for oils, trace metals, moisture sorption and possible adsorption of the active to carrier surfaces. For microbial products, viable count alone may be insufficient; germination, sporulation, infectivity,

colonization or target-specific bioassay may reveal sublethal damage.

Successful formulation of biological agricultural products requires simultaneous optimization of interactions among the active ingredient, surfactant system, and carrier or inert matrix. These interactions determine wetting and dispersion, emulsion or suspension stability, rheological behavior, active-ingredient integrity, microbial viability, biological efficacy, and storage stability. Excipient selection must satisfy physicochemical and biological compatibility while also meeting regulatory acceptability, purity

specifications, environmental-safety expectations, and the intended agricultural use pattern. Accordingly, surfactants and carriers should be treated as integral design variables rather than functionally inactive additives. A useful development sequence is to screen individual excipients, challenge the complete formulation under storage and

dilution conditions, and then confirm biological potency after exposure. The interdependence of the active ingredient, surfactant, and carrier, together with the major physical, biological, and regulatory constraints governing their selection, is summarized in Table 2 and Fig. 2.

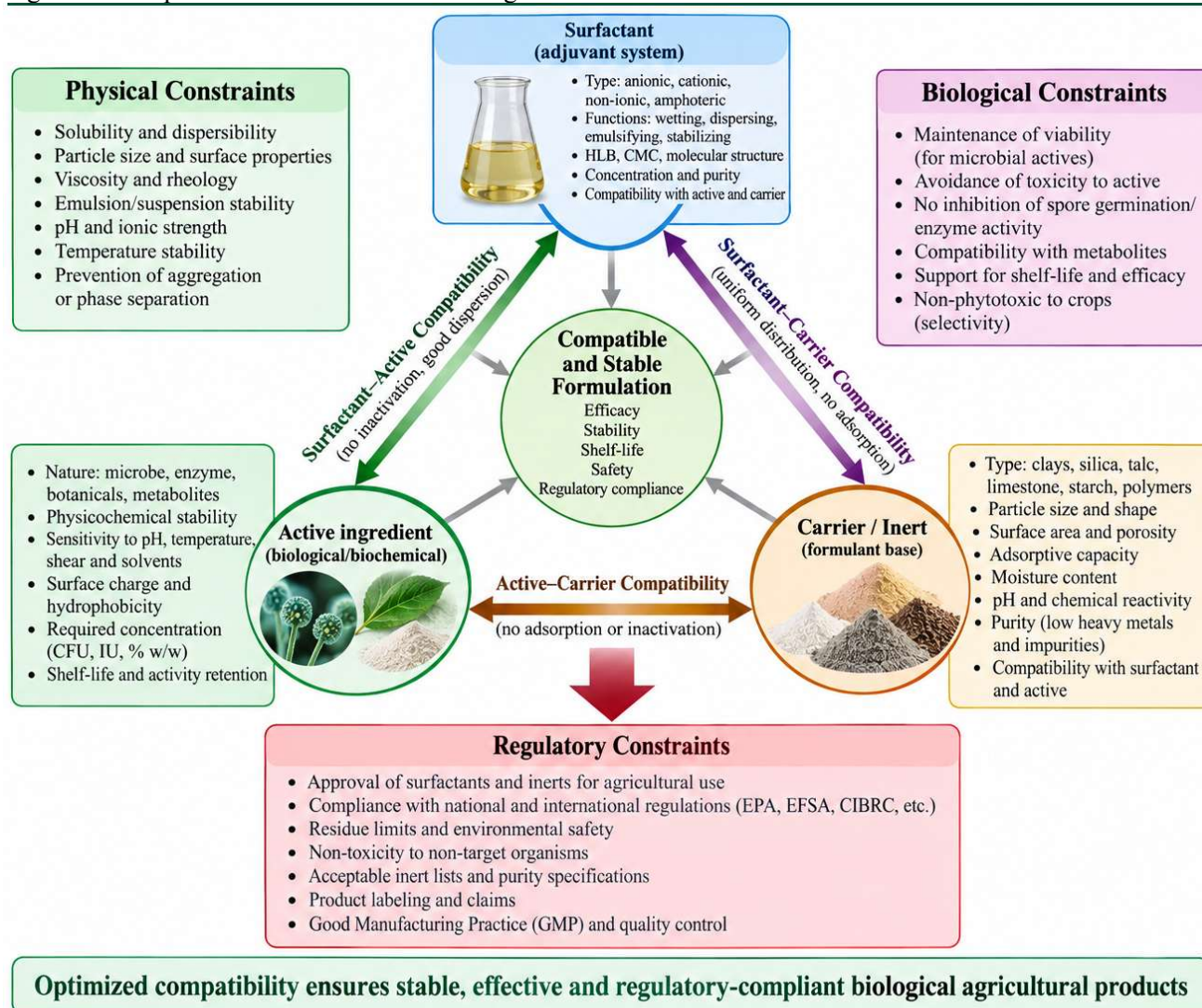


Fig. 2. Surfactant-active ingredient-carrier compatibility framework illustrating the major physical, biological, and regulatory constraints governing the development of stable, efficacious, and registration-ready biological agricultural formulations.

Regulatory acceptability of inerts must be checked early. A technically excellent surfactant can become commercially unusable if it lacks an appropriate regulatory status for the intended crop, geography or food-use pattern. Composition disclosure, impurity profiles and supplier change control are therefore part of regulatory-quality formulation development. U.S. pesticide registration, for example, requires formulation and product-chemistry information and addresses inert ingredients within the registration framework (U.S. EPA 2026).

6. Scale-Up and Manufacturing Process Development

Scale-up should preserve the critical process conditions that control product quality, not merely reproduce laboratory ingredient percentages. Relevant variables include impeller type, power per unit volume, tip speed, mixing time, order of addition, milling energy, temperature history, oxygen transfer, vacuum exposure, homogenization pressure, drying inlet/outlet temperature, residence time and humidity. A laboratory process that uses a rotor-stator

homogenizer may not translate directly to a large tank equipped with an anchor or turbine mixer.

For fermentation-derived products, upstream and downstream operations are coupled. Recent analyses of microbial biopesticide production similarly identify fermentation productivity, propagule quality, recovery, stabilization and scalable formulation as interdependent determinants of commercial performance (Verma et al. 2024; Glare et al. 2026). Fermentation endpoint affects cell physiology, spore robustness, metabolite profile and broth rheology. Downstream concentration by centrifugation, filtration or membrane processes can impose shear and osmotic stress. Spray drying is scalable but may reduce viability of heat-sensitive organisms; freeze drying can preserve activity but is often expensive; fluid-bed drying and low-temperature air drying can offer intermediate solutions. Protective excipients should be optimized with

the drying process rather than after it (Morgan et al. 2006; Fu and Chen 2011).

Commercial translation requires coordinated scale-up across active-ingredient production, downstream recovery, formulation, packaging, stability assessment, quality assurance, and regulatory registration. Each stage can alter potency, physicochemical stability, shelf life, manufacturing reproducibility, regulatory compliance, and cost. Scale-up should therefore be managed as an integrated development pathway rather than as enlargement of isolated unit operations. In practice, scale-dependent failure modes should be identified prospectively and linked to measurable critical process parameters and release criteria. The interrelationship among these stages, together with the cross-cutting roles of analytical control, surfactant and inert compatibility, process economics, environmental safety, and regulatory support, is illustrated in Fig. 3 and Table 3.

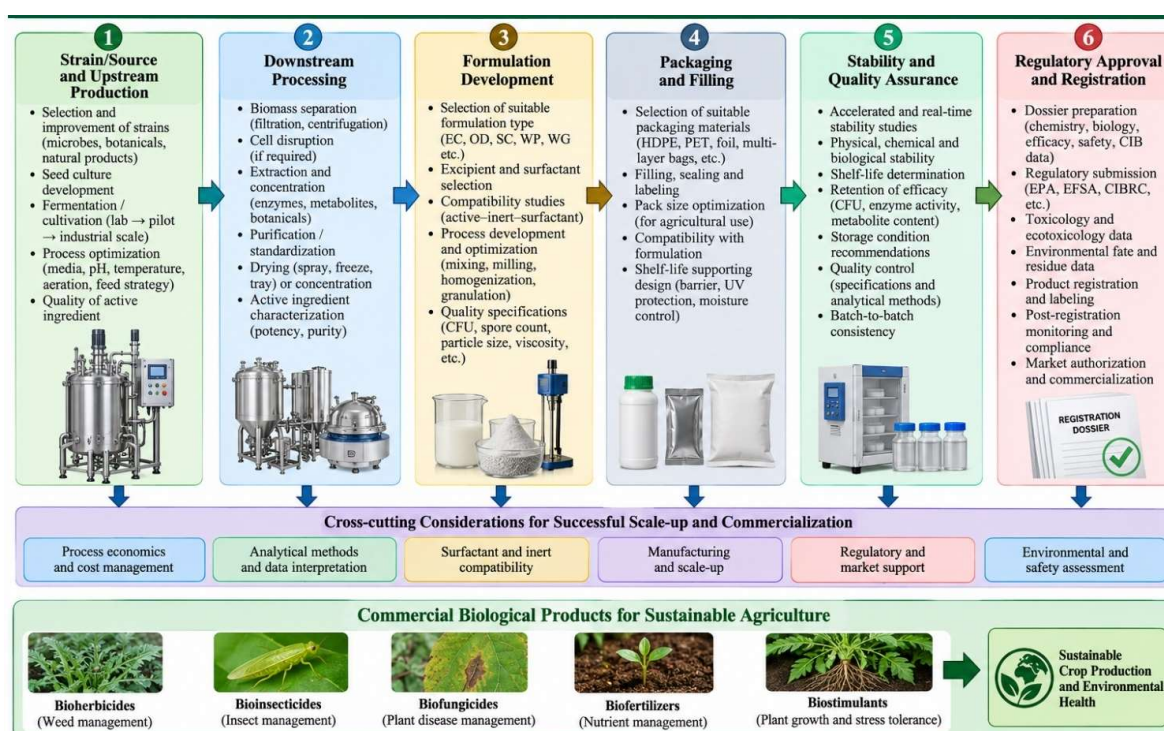


Fig. 3. Integrated scale-up pathway linking fermentation/active-ingredient production, downstream processing, formulation development, packaging, stability and quality assurance, and regulatory registration for biological agricultural products, including biopesticides, biofertilizers, and biostimulants.

Table 3. Stage-gated scale-up framework

Stage	Typical scale	Primary objective	Critical measurements	Release decision	Common failure
Bench	0.1–5 L/kg	Proof of formulation concept	Compatibility, pH, PSD, viscosity, viability/potency	Select 2–3 prototypes	Optimizing only initial efficacy
Pilot	10–200 L/kg	Establish process window	Mixing/shear, heat, milling, drying, yield, contamination	Lock critical process parameters	Direct volumetric scale-up
Engineering	0.2–2 m ³ /t	Equipment translation	Batch time, energy, transfer losses, cleaning, packaging	Confirm reproducibility	Ignoring hold times and transfer shear

Stage	Typical scale	Primary objective	Critical measurements	Release decision	Common failure
Commercial	Multi-m ³ /t	Routine reproducible manufacture	IPC, yield, specifications, deviations, stability	Validated/controlled production	Supplier and raw-material variability

7. Quality by Design and Product Specifications

A useful development approach is to define a quality target product profile and identify critical quality attributes (CQAs), critical material attributes and critical process parameters. CQAs differ by biological class. For a fungal bioherbicide, they may include species/strain identity, conidial concentration, germination, moisture, contamination, particle-size behavior and weed-control potency. For a botanical bioinsecticide, they may include marker-compound content, impurity profile, emulsion or suspension behavior and insecticidal potency. For a biofertilizer, viable count, identity, contaminant limits, pH, carrier moisture and plant-growth functional performance are central.

Specifications should be scientifically linked to field performance. Tight control of a parameter that has no demonstrated relationship to efficacy increases cost without necessarily increasing quality, whereas omission of a performance-relevant attribute creates risk. Development batches should therefore be used to build correlations among physicochemical properties, biological potency, storage stability and application behavior.

8. Analytical Interpretation for Development and Release

8.1 Identity, viable count and biological potency

Microbial identity can be supported by phenotypic characterization and molecular methods such as species- or strain-relevant PCR and sequencing. Viable counts may be measured by colony-forming units, spore counts combined with germination, most-probable-number methods or other validated approaches. Interpretation requires caution: total particle or cell counts can substantially exceed viable counts, while CFU can underestimate clumped organisms. Potency bioassays remain important because viability does not guarantee target activity.

8.2 Particle size, zeta potential and rheology

Laser diffraction reports a distribution rather than a single particle size; D10, D50 and D90 should be interpreted together with microscopy and storage behavior. A decrease in apparent particle size after aggressive milling may improve suspensibility but damage spores or increase Ostwald ripening risk for crystalline actives. Zeta potential can indicate electrostatic stabilization but is not a universal stability threshold, particularly when polymeric steric stabilizers dominate. Rheological data should include shear-

rate dependence, yield behavior and thixotropy when settling and redispersibility are relevant.

8.3 Chemical assay and chromatographic fingerprints

HPLC, UHPLC, GC, LC-MS and GC-MS are useful for botanical and fermentation-derived products. Marker selection should reflect activity and manufacturing consistency. A chromatographic fingerprint can be more informative than a single marker when multiple constituents contribute to efficacy. Method validation or fit-for-purpose verification should address specificity, linearity, precision, accuracy/recovery, range, robustness and sample stability. Degradation products observed during accelerated stability should be interpreted in relation to potency and safety rather than treated solely as analytical anomalies.

8.4 Stability interpretation

Accelerated stability is a development tool, not a substitute for appropriately designed real-time data where required. Biological decay may be non-linear and highly temperature dependent. Viability, moisture, water activity, pH, viscosity, phase separation, particle-size drift, marker assay and bio-efficacy should be trended together. Packaging must be included because oxygen transmission, water-vapor transmission, light exposure and sorption into container materials can dominate shelf life.

9. Application-Specific Formulation Strategy

9.1 Bioherbicides

Bioherbicides face a difficult delivery environment because weed foliage is often waxy, variable in orientation and exposed to rapid drying, UV radiation and rainfall. The persistent scarcity of widely successful microbial bioherbicides has been linked to inconsistent field performance, formulation limitations, production economics and regulatory/commercial barriers, reinforcing the need to integrate delivery design with biological mode of action (Duke 2024). Indigenous-isolate and metabolite-based mycoherbicide programs, including those targeting invasive weeds such as Lantana, face the same constraints and have been reviewed from the standpoints of product development and sustainable use (Singh and Pandey 2019b, 2022a, 2025b, 2025c, 2025d). Formulations should maximize deposition and maintain a favorable microenvironment long enough for infection or phytotoxin action. Oil dispersions and selected emulsifiable systems

can improve cuticular contact for compatible fungal propagules or lipophilic metabolites, whereas WP and WG can provide storage stability for robust spores. Humectants and oils may improve efficacy but must be balanced against crop safety and sprayability.

9.2 Bioinsecticides

For entomopathogenic fungi, formulation can influence conidial adhesion, germination and penetration of the insect cuticle. Oil-based formulations have often been used to improve application under low-humidity conditions. *Bacillus thuringiensis* products commonly exploit stable spores and crystalline proteins in dry or suspension systems, while baculoviruses require protection from UV and appropriate deposition on feeding surfaces (Lacey et al. 2015; Mascarin and Jaronski 2016).

9.3 Biofungicides and bacterially based disease-control products

Biocontrol agents used against plant disease must arrive at the infection court, colonize the relevant niche and remain physiologically active. Seed-treatment formulations require adhesion without reducing seed germination; foliar products require spray stability and survival; soil products require compatibility with irrigation water and rhizosphere conditions. *Bacillus* spores offer formulation advantages because of their robustness, whereas non-spore-forming bacteria can require more protective liquid or dry matrices.

9.4 Biofertilizers

Biofertilizer formulation is strongly influenced by inoculation route. Seed inoculants require high cell density, adhesion and short-term survival on seed; soil and in-furrow products require compatibility with water and fertilizers; carrier-based powders require controlled moisture and sterility or low contaminant burden. Liquid inoculants can simplify application but may require osmoprotectants and careful preservation. Carrier-based inoculants remain important where cold-chain infrastructure is limited (Bashan et al. 2014).

9.5 Biostimulants

Biostimulant formulations range from microbial suspensions to concentrated seaweed, humic and protein-

hydrolysate liquids and dry soluble/dispersible products. Because the regulatory identity of a biostimulant is tied to stimulation of plant processes rather than pesticidal action, claims and analytical specifications must be aligned. Complex extracts require raw-material standardization, manufacturing fingerprints and biologically meaningful markers (du Jardin 2015; Roupahel and Colla 2020).

10. Regulatory Support and Product Registration

Regulatory strategy should be established before final formulation lock because a change in solvent, surfactant, preservative, manufacturing process or active source can trigger new data or bridging requirements. Recent safety-focused literature also argues that microbial pesticide development should connect product characterization and efficacy with proportionate assessment of human, animal and environmental risks across the product life cycle (Cai and Dimopoulos 2025). In the United States, EPA distinguishes microbial and biochemical pesticides and specifies registration data requirements under 40 CFR Part 158, including microorganism-specific requirements for microbial pesticides. Product chemistry, composition, manufacturing information, toxicology and other data are considered according to use pattern, and efficacy data must be generated and maintained even where routine submission is not required for non-public-health uses (U.S. EPA 2026).

In the European Union, plant-protection products containing microorganisms are evaluated under Regulation (EC) No. 1107/2009 and microorganism-specific implementing rules that became applicable in 2022. Commission Regulation (EU) 2022/1440 specifies product data requirements for plant-protection products containing microorganisms, while Regulation (EU) 2022/1441 updates the uniform principles for evaluation and authorization. These rules emphasize biological properties of microorganisms and risk assessment appropriate to microbial active substances (European Commission 2022a, 2022b). In India, biostimulants were brought under the Fertilizer (Control) Order, 1985 through the 2021 regulatory framework; the government has subsequently clarified quality regulation under Clause 20C (Government of India 2025). Product developers must distinguish biostimulant, fertilizer and pesticidal claims because classification determines the dossier and authority (Table 4).

Table 4. Registration-support dossier elements that should be connected to formulation development

Dossier element	Formulation-development output	Why it matters	Typical risk if delayed
Identity/composition	Active identity, concentration, full formulation composition, impurity profile	Defines product and supports reproducibility	Late reformulation
Manufacturing process	Flow diagram, process controls, in-process tests	Connects scale-up with registered product	Uncontrolled batch variability

Dossier element	Formulation-development output	Why it matters	Typical risk if delayed
Product chemistry	pH, density, viscosity, PSD, suspensibility/emulsion/disintegration, moisture	Demonstrates physical quality	Registration questions and field failures
Analytical methods	Validated/verified active, marker, viable-count and contaminant methods	Enables release and stability testing	Inability to defend specifications
Stability	Real-time/accelerated trends in package	Supports shelf life	Overstated expiry
Efficacy	Dose-response and multi-environment performance	Supports label claims	Commercial underperformance
Safety/non-target	Toxicology/ecotoxicology and relevant exposure information	Supports safe use	Rework after formulation lock
Label/use pattern	Crop, target, dose, timing, equipment, precautions	Determines exposure and data needs	Mismatch between data and intended market

11. Cost Management and Techno-Economic Considerations

Cost management should start during formulation screening. Cost of goods is determined by active yield, fermentation productivity, downstream recovery, drying, formulation excipients, batch cycle time, labor, utilities, quality testing, packaging, storage and logistics. A formulation with expensive excipients can still be commercially superior if it increases shelf life, removes refrigerated distribution, lowers application dose or reduces product returns. Low-cost agricultural and industrial residues can lower fermentation-media cost and support circular-economy objectives, although variable composition

complicates quality control (Singh and Pandey 2026). Conversely, a low-cost carrier can become expensive if it causes rapid viability loss or requires high field rates.

A useful metric is cost per treated hectare rather than cost per kilogram or liter of product. This integrates potency, formulation concentration, recommended dose and application frequency. Manufacturing yield should be calculated across the complete process, including fermentation, harvest, drying, blending and packaging losses. Sensitivity analysis should identify whether profitability is most influenced by fermentation yield, drying recovery, raw-material price, packaging, plant utilization or field dose (Table 5).

Table 5. Practical cost levers in biological-product commercialization

Cost driver	Technical lever	Potential benefit	Trade-off to monitor
Fermentation	Higher titer/productivity; shorter cycle	Lower vessel and utility cost per unit active	May alter propagule quality/metabolite profile
Recovery	Higher capture yield; fewer unit operations	Reduced active loss	Purity and contamination risk
Drying	Optimize solids and protective matrix	Longer shelf life; lower freight	Energy and viability loss
Formulation	Increase active loading	Lower packaging/freight per treated hectare	Physical stability and dose accuracy
Packaging	Right-size barrier performance	Avoid over-engineering	Shelf-life failure if barrier inadequate
QC	Risk-based methods and sampling	Lower release cost and cycle time	Insufficient control if poorly justified
Field dose	Improve deposition/persistence	Lower cost per hectare	Crop safety and non-target exposure

12. Integrated Development Workflow

A commercially disciplined program can be organized into eight linked steps: (i) define the target product profile and regulatory classification; (ii) characterize the active ingredient and its failure modes; (iii) screen formulation platforms and inerts for physical and biological compatibility; (iv) optimize the lead formulation using statistically designed experiments; (v) establish analytical methods and provisional specifications; (vi) scale to pilot manufacture while mapping critical process parameters; (vii) generate stability, efficacy, safety and registration-support data on representative product; and (viii) conduct techno-economic analysis and commercial manufacturing confirmation. The key principle is that formulation, analytics, regulation and economics should advance in parallel.

Commercial development of biological agricultural products is most effectively managed through a stage-gated

framework in which technical, regulatory, and commercial requirements are evaluated progressively from discovery to market launch. The process begins with establishment of a quality target product profile (QTPP) defining intended use, formulation type, application route, shelf-life target, performance requirements, and commercial objectives. Subsequent stages integrate identification of critical quality attributes (CQAs), formulation and process optimization, analytical-method development and validation or fit-for-purpose verification, stability assessment, efficacy and crop-safety evaluation, toxicological and environmental risk assessment, scale-up, cost analysis, and preparation of the regulatory dossier. Advancement should occur only when predefined technical and commercial criteria are satisfied. This stop/go discipline is particularly important for biological products because an apparently successful efficacy prototype may still fail through loss of viability or potency, unacceptable storage behavior, non-scalable

processing, regulatory incompatibility, or excessive cost per treated hectare. An integrated stage-gated commercialization framework is presented in Fig. 4.

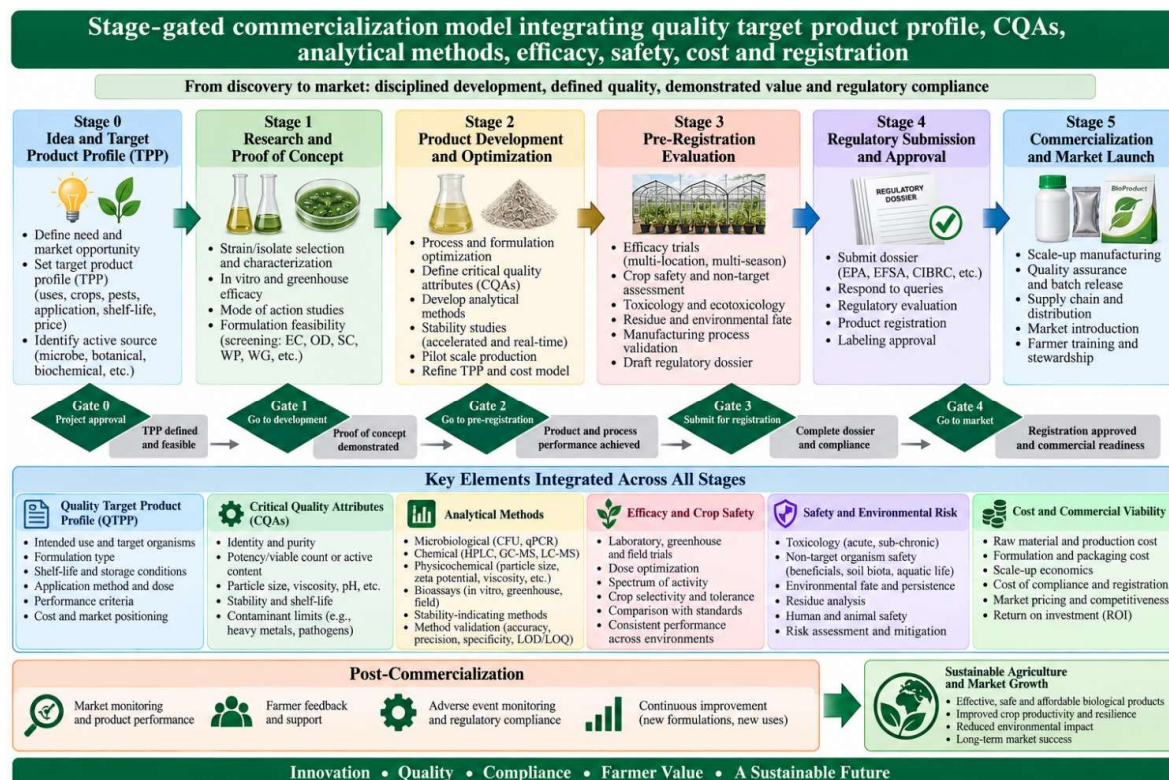


Fig. 4. Stage-gated commercialization model for biological agricultural products integrating the quality target product profile (QTPP), critical quality attributes (CQAs), formulation and process development, analytical methods, stability, efficacy and crop safety, environmental and toxicological assessment, cost and commercial viability, regulatory registration, market launch, and post-commercialization monitoring.

13. Emerging Formulation Technologies

Microencapsulation, polymeric matrices, lipid carriers, Pickering emulsions, nanoemulsions and controlled-release particles are increasingly investigated to protect biological actives from UV, oxidation, desiccation and wash-off (Gundreddy et al. 2024; Senthil-Nathan et al. 2026). These systems can improve persistence but introduce new questions regarding manufacturing complexity, particle characterization, environmental fate, regulatory acceptability and cost. Advanced delivery should therefore be adopted when it solves a clearly defined product limitation rather than simply because it is technologically novel.

Digital formulation development is also expanding. Multivariate analysis can relate formulation composition and process parameters to stability and potency, while mechanistic and data-driven models can support scale-up. High-throughput compatibility screening, automated imaging of physical stability and predictive shelf-life modeling may shorten development cycles, provided models are anchored to biologically meaningful endpoints.

14. Research Gaps and Future Priorities

Major research priorities include standardized methods that link viable count or chemical potency with field performance; predictive models for microorganism–surfactant interactions; improved understanding of water activity and glass-transition behavior in dry microbial formulations; scalable, low-energy drying; potency-linked marker strategies for complex fermentation and botanical products; harmonized interpretation of formulation changes across regulatory jurisdictions; and transparent techno-economic benchmarks for biological manufacturing. A further priority is prospective validation of formulation decision frameworks against commercial development outcomes, because laboratory physical stability alone is an inadequate surrogate for field robustness or market readiness. For weed biocontrol in particular, formulation research should address short leaf-wetness periods, UV exposure, rainfastness, and inconsistent penetration while preserving crop selectivity. Cell-free fungal products may reduce dependence on viability and humidity but shift development priorities toward metabolite stabilization,

marker-linked potency, manufacturing consistency, and scalable fermentation (Singh and Pandey 2025a, 2025c, 2025d, 2026).

15. Conclusions

Formulation is the central translation step that converts biological activity into a reproducible agricultural product. EC, OD, SC, WP, and WG technologies each offer distinct advantages, but their suitability depends on whether the active is a living microorganism, spore, virus, botanical compound, fermentation metabolite, or complex biostimulant. Surfactant and inert selection must therefore integrate physical chemistry with biological compatibility, while scale-up must preserve critical quality attributes through controlled mixing, shear, drying, holding, and packaging. Analytical methods should distinguish identity, viability, potency, and physical performance and should be linked to specifications that are meaningful for field use. Regulatory support is most efficient when composition, manufacturing, specifications, stability, efficacy, and safety are developed as a connected evidence package rather than as separate late-stage activities. Commercial decisions should likewise be based on reliable performance per treated hectare and shelf-life value rather than ingredient cost alone. The principal implication of this review is that successful biological products emerge from concurrent optimization of formulation, process engineering, analytics, regulation, and economics. Applying this integrated, stage-gated approach should improve the probability that promising biological actives progress from laboratory efficacy to robust, scalable, registration-ready, and commercially viable agricultural products.

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