FORMULATION CHOICE

How and why they are chosen

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On behalf of ECPA Specification Expert Group

Topics

- Why formulate?
- How to identify formulation options
- Drivers
- Principle formulation type overview
- Phys-chem quality tests overview

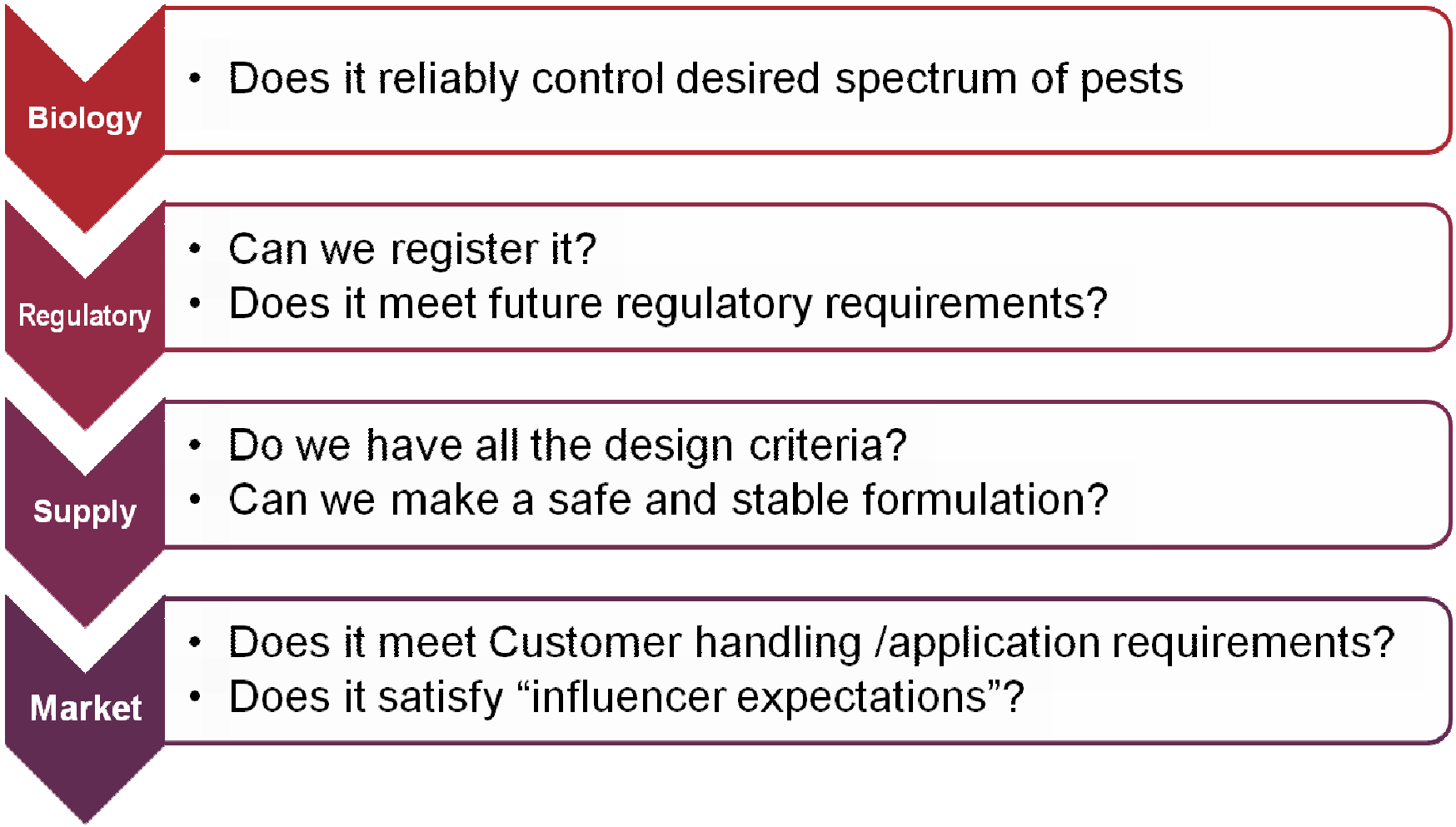
Why formulate?

- To allow an even application over target area
- To optimise biological effectiveness of AI.
- To improve product handling and application
- To improve safety and convenience to user
- To ensure safety in manufacture and use
- To maximise pack stability and ease of disposal
- To provide competitive edge for products
- To extend life cycle of active ingredient – mixes, new technologies etc.

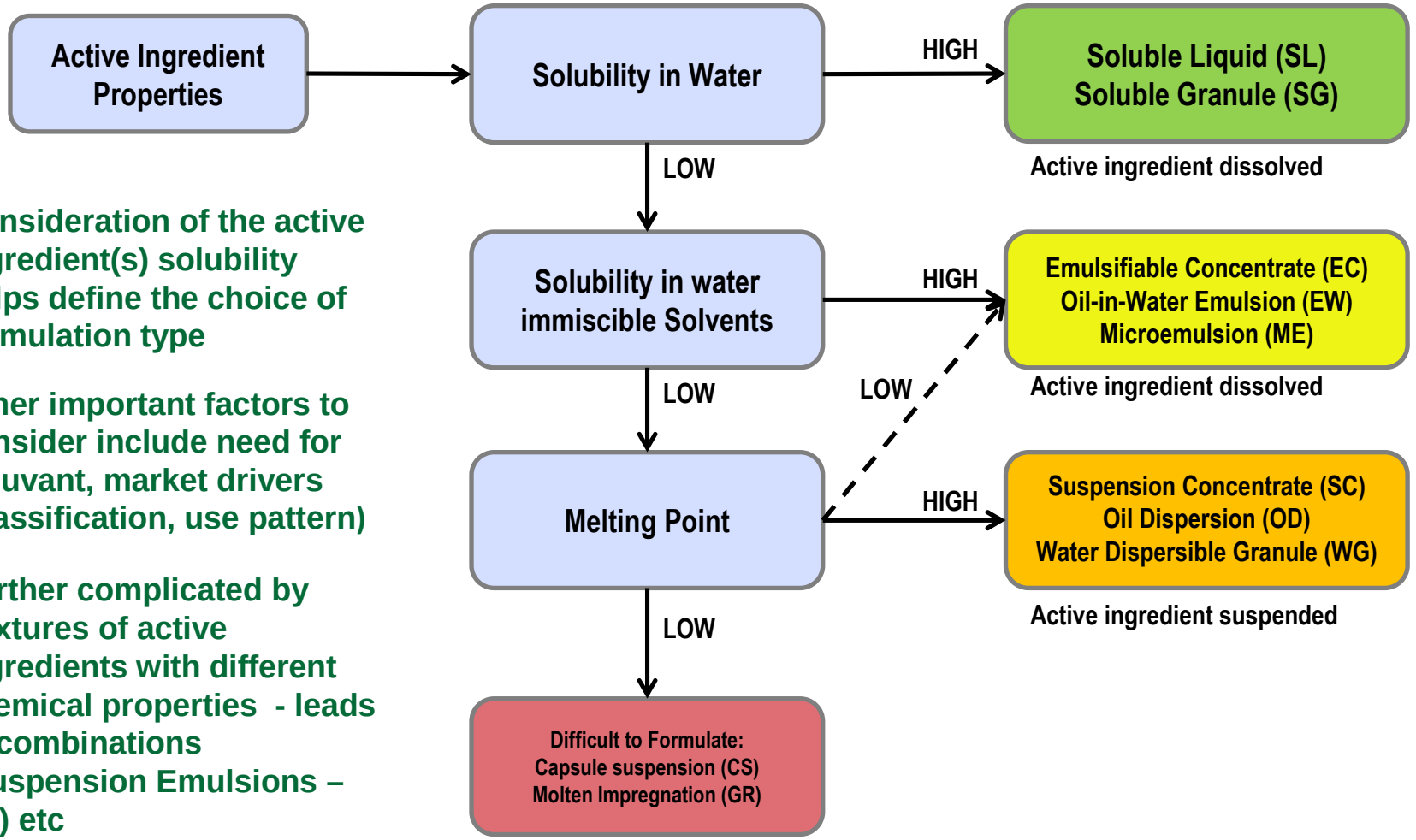
What affects the choice of formulation type?

- Phys/chem props of ai (or combinations of ai's)
- Efficacy needs e.g. built in adjuvant, solvent etc.
- Use pattern/applicn technology (e.g. spray drift)
- Environmental effects (e.g. Residues, leaching)
- Ease of use (Kg/Ha)
- Safe handling/Hazard classification
- Transport & storage
- Cost
- Ease of Manufacture
- Prior art – Patents!

Formulation Design - Drivers



Formulation Driver: Phys/Chem Properties



Consideration of the active ingredient(s) solubility helps define the choice of formulation type

Other important factors to consider include need for adjuvant, market drivers (classification, use pattern)

Further complicated by mixtures of active ingredients with different chemical properties - leads to combinations (Suspension Emulsions – SE) etc

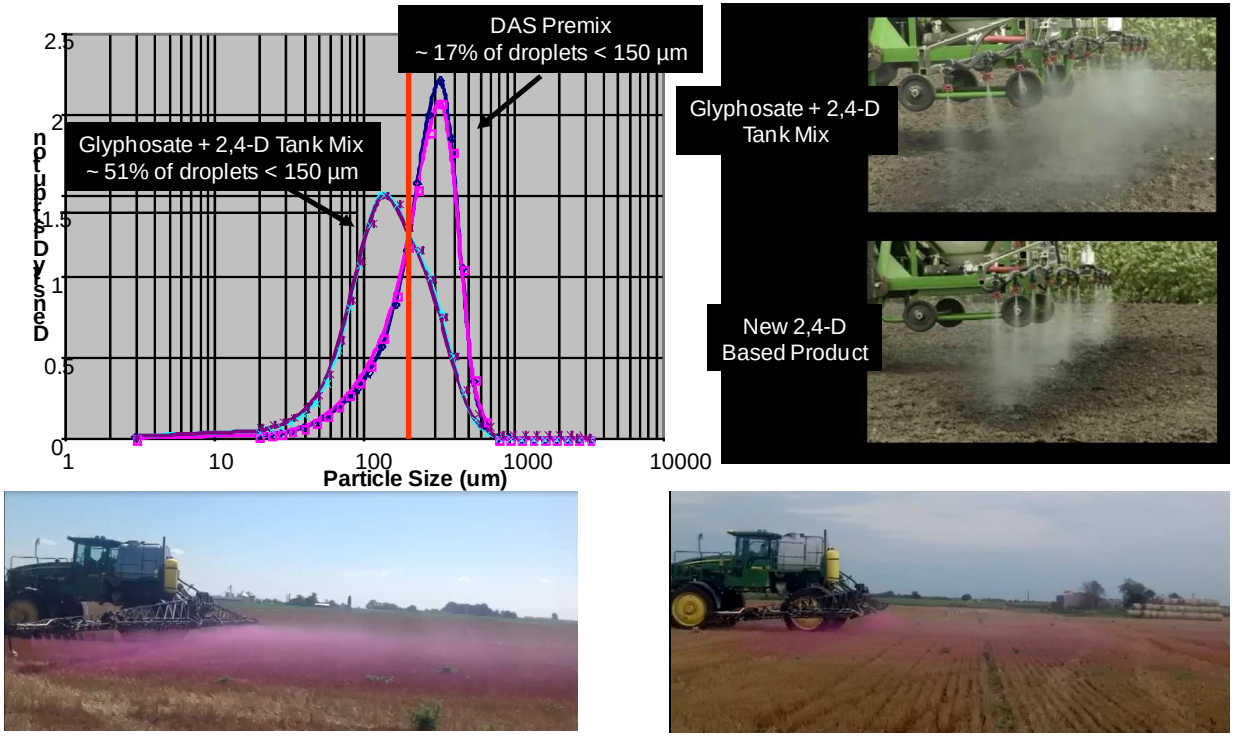
Principal Formulation Types

Aqueous solution	**SL**
Emulsifiable Concentrate	**EC**
Emulsifiable Granule	**EG**
Suspension Concentrate	**SC**
Water Dispersible Granule	**WG**
Wettable Powder	**WP**
Granule	**GR**

Oil in water emulsion	**EW**
Suspension Emulsion	**SE**
Microemulsion	**ME**
Oil Dispersions	**OD**
Capsule Suspension	**CS**
Ultra Low Volume	**UL**
"Z" mixtures	**ZC, ZE, ZW**

Effect of Application and Field Usage on Formulation Type

- Spray drift
  - If drift is of major concern then consider built in drift control agents or recommend use of additives and/or appropriate spray nozzles.
  - Built in drift control agent chemistry might dictate formulation choice.



Effect of Application and Field Usage on Formulation Type

- Bulk storage needs – ISO, IBC, on farm
- Ability to add through induction bowl/chem-handler
- Tank mix requirements
- Tank cleaning needs
  - E.g. easier to wash out SL residue than particulate residue

Formulator's Toolbox

- Significant reduction of raw materials available to chemist (e.g. NMP, DMF, aromatic solvents etc)
- Re-evaluations, chemical registration, new data etc
- Huge burden (resource, cost, time) on industry to reformulate
- Need pragmatic approach from authorities where reformulation has lead to less hazardous formulation (e.g. reduced data requirements, reduced time to approval, letter approval only in some cases)

Governmental Drivers

Global
- GHS

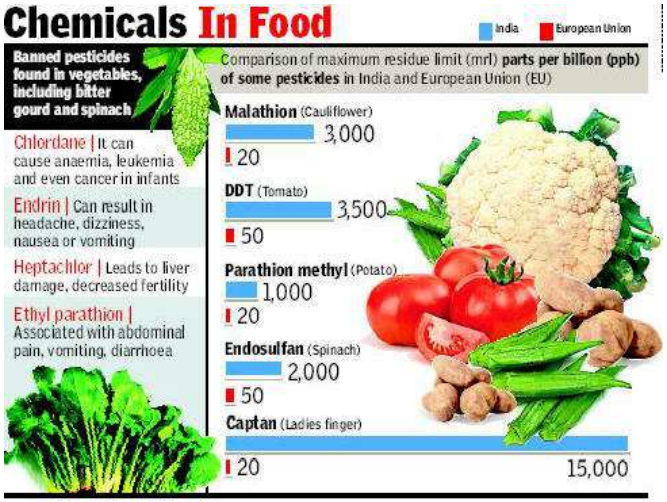
EU
- 1107/2009, REACH, biocide directive, DPD, PPP comparative assessment
- Classification, Labeling and Packaging Regulation 1272/2008

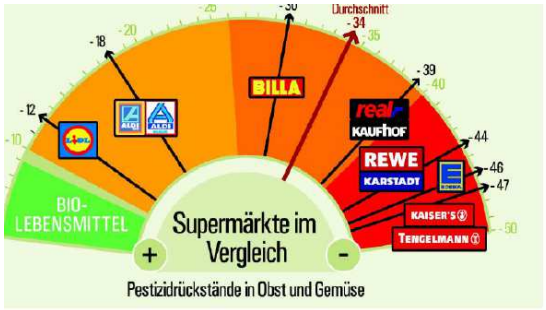
NA/LA
- FQPA, TSCA
- Brazil, Eye Opacity Requirements

Pacific
- China's 12th Five Year Plan
- Joint MIIT Industrial Policy

Non-governmental Drivers

- Growth in GMO crops
- Non governmental organizations
- Supermarkets
- Consumer associations





Non-governmental Drivers (cont)

Other Influencers

- Grower Convenience
- Organic Foods
- Market Dynamics

Principal Formulation Types

Principal Formulation Types

Aqueous solution	SL
Emulsifiable Concentrate	EC
Suspension Concentrate	SC
Suspension Emulsion	SE
Oil Dispersions	OD
Water Dispersible Granule	WG
Granule	GR
Oil in water emulsion	EW
Microemulsion	ME
Emulsifiable Granule	EG
Wettable Powder	WP
Capsule Suspension	CS
Ultra Low Volume	UL
"Z" mixtures	ZC, ZE, ZW

Soluble Liquid (SL)

Description:

Water based formulation where salt of pesticide acid is dissolved in water. May also contain adjuvant (wetting agent) to help wetting of leave surfaces.

Advantages

- No flash point
- Easy to manufacture
- Low cost
- Compatible with HDPE packaging

Disadvantages

- Acid form can show weaker biological activity compared to ester
- Can have high eye irritancy (unacceptable C+L)

Soluble Liquid (SL)

Salt formulation dissolved in water and further diluted in water for application

Resulting solution is clear and infinitely dilutable

Product **Dilution** **Spray Solution**

Component	Typical Loading (g/L)
Active ingredient	50 - 600
Conjugate base	50 - 500
Adjuvant	0- 100
Buffer / sequestrant	0 - 30
Water (polar solvent)	Balance

Emulsifiable Concentrate (EC)

Description:

Single phase formulation where the active ingredient is dissolved in solvent and forms emulsion when diluted in water

Advantages

- High ai content often possible
- Easy to manufacture
- Easy to use
- Adjuvants easy to incorporate
- Relatively cheap to manufacture
- Can use “green” solvents

Disadvantages

- High solvent content (C+L issues)
- Low flash point
- Skin penetration and eye irritation
- Low temperature stability (crystallisation)
- Potential for phytotoxicity

Emulsifiable Concentrate (EC)

Emulsifiable concentrate formulations are diluted in water for application.

Upon dilution, they form a characteristic white emulsion consisting of droplets of the EC formulation in water

Component	Typical Loading (g/L)
Active ingredient	50 - 500
Emulsifiers	50 - 150
Co-solvent	0 - 200
Solvent	Balance

Suspension Concentrates (SC)

Description:

Multiphase formulation where the active ingredient is suspended in water

Advantages

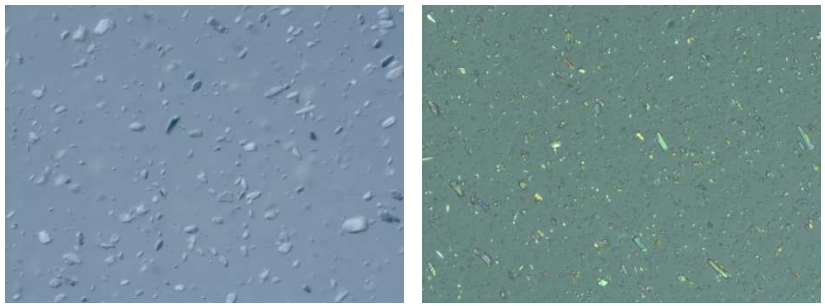
- Aqueous based
- Higher or no flash point
- Low cost formulation (high load, water based)
- Existing, known technology
- Low skin penetration

Disadvantages

- Physical instability on storage (settling, syneresis)
- Potential tank mix compatibility issues
- Higher viscosity can give issues with pouring / rinsing

Suspension Concentrate (SC)

SC formulations are opaque suspensions of active ingredient suspended in water, applied by further dilution in water



Component	Typical Loading (g/L)
Active ingredient	50 - 600
Wetting agent	5 - 15
Dispersing agent	20 -50
Antifreeze	50 - 100
Antifoam	1 -2
Biocide	1 -2
Rheology aids	1 - 5
Water	Balance

Suspension Emulsion (SE)

Description:

Multiphase formulation whereby an emulsified active is combined with active suspended in water

EW (EC) + SC

Advantages

- Allows mixtures of active ingredients with different properties
- Higher or no flash point
- Reduced skin penetration (than EC)
- Reduced solvent concentration

Disadvantages

- Complex technology with long development time
- Expensive and complex to manufacture
- Physical instability on storage (settling, syneresis)
- Viscosity / ease of pouring

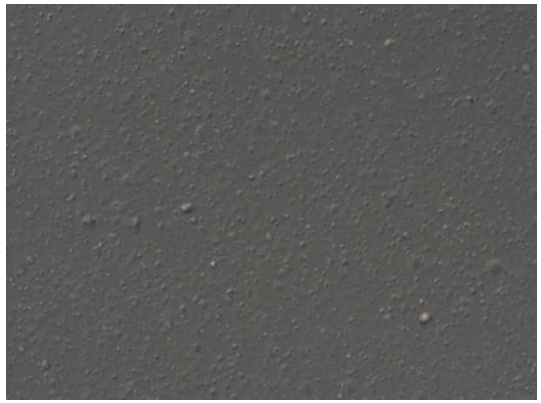
Suspension Emulsion (SE)

Also referred to as Suspo Emulsions, they consist of suspended particles in a water based macro emulsion

Diluted in water for application

Component	Typical Loading (g/L)
Active ingredient	100 - 600
Wetting + Dispersing agent	40 - 80
Solvent	0 - 300
Antifreeze	50 - 100
Antifoam	1 -2
Biocide	1 -2
Rheology aids	1 - 5
Water	Balance

Under microscope, can see individual solid particles dispersed amongst emulsion droplets



Oil Dispersion (OD)

Description:

Multiphase formulation where the active ingredient is suspended in oil

Advantages

- Can formulate active with low solvent solubility in oil based formulation
- Built in adjuvant
- Can use natural seed oils (non aromatic)

Disadvantages

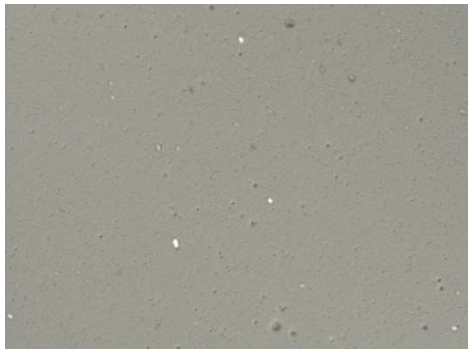
- Physical instability on storage (settling, syneresis)
- Tank cleaning can be an issue
- Bulk storage difficult

Oil Dispersion (OD)

Oil based formulation containing suspended solid particles of active ingredient

Applied by dilution in water producing a dilute white suspension emulsion

If diluted in oil = OF (oil flowable)



Component	Typical Loading (g/L)
Active ingredient	20 - 600
Emulsifiers	5 - 150
Hydrophobic silica	2 - 60
Oil (solvent)	Balance

Water Dispersible Granules (WG)

Description:

Solid formulation containing agglomerates of active ingredient that disperse to primary particles on dilution in water

Advantages

- Low dust (extrusion)
- Easy to package
- High active content
- No flash and reduced C+L

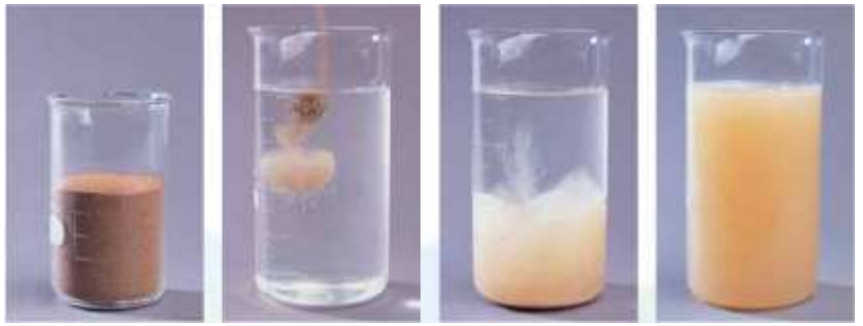
Disadvantages

- Can be expensive to manufacture
- Poor dispersion in water can occur
- Tank mix compatibility with other products can be an issue
- Dosing by farmer is difficult (low use rates)

Water Dispersible Granule (WG)

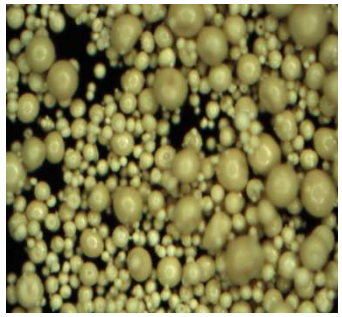
WG formulations are diluted in water for application.

On dilution, the granules disintegrate and disperse to give a homogenous suspension



Component	Typical Loading (%)
Active ingredient	50 - 90
Dispersing / binding agent	5-20
Wetting agent	1 - 5
Antifoam	0 - 1
Disintegrating agent / filler	Balance

Extrusion



Spray Dried

Granule (GR)

Description:

Solid granule formulation for direct application

Advantages

- Ready to use
- Low drift hazard
- Penetrate dense foliage
- Usually requires simple application equipment

Disadvantages

- Will not stick to target
- No folia use with herbicides
- May need to incorporate into soil
- May require moisture to activate

CIPAC Tests for Key Liquid Formulation Types

Test Description	CIPAC number	Formulation Type					
		SC	SE	CS	SL	EC/ME	OD
Active ingredient content	Company method	√	√	√	√	√	√
-- free active ingredient content	Company method	n/a	n/a	√	n/a	n/a	n/a
-- Release rate of active ingredient	Company method	n/a	n/a	√	n/a	n/a	n/a
pH or acidity alkalinity	MT 75.3 or MT 191	√	√	√	√	√	√
Pourability	MT 148.1	√	√	√	n/a	n/a	√
Suspensibility	MT 184	√	n/a	√	n/a	n/a	n/a
Wet sieve	MT 185	√	√	√	n/a	n/a	√
Spontaneity	MT160	√	n/a	√	n/a	n/a	n/a
Dispersion stability	MT 180	n/a	√	n/a	n/a	n/a	√
Solution Stability	MT 41	n/a	n/a	n/a	√	n/a	n/a
Emulsion characteristics	MT 36.3	n/a	n/a	n/a	n/a	√	n/a
Persistent foam	MT 47.2	√	√	√	√	√	√
Cold Stability	MT 39.3	√	√	√	√	√	√
Elevated temperature stability	MT 46.3	√	√	√	√	√	√

CIPAC Tests for Key Solid Formulation Types

Test Description	CIPAC number	Formulation Type					
		WP	SP	WG	SG	EG	GR
Active ingredient content	Company method	√	√	√	√	√	√
pH or acidity alkalinity	MT 75.3 or MT 191	√	√	√	√	√	√
Pour and tap density	MT 186	n/a	n/a	n/a	n/a	n/a	√
Nominal size range	MT 58	n/a	n/a	n/a	n/a	n/a	√
Suspensibility	MT 184	√	n/a	√	n/a	n/a	n/a
Dispersion stability	MT 180	n/a	n/a	n/a	n/a	√	n/a
Wet sieve	MT 185	√	n/a	√	n/a	√	n/a
Attrition Resistance	MT 179	n/a	n/a	√	√	√	√
Dustiness	MT 171	n/a	n/a	√	√	√	√
Degree of dispersion	MT 174	n/a	n/a	√	n/a	n/a	n/a
Wettability	MT 53.3	√	√	√	n/a	√	n/a
Flowability	MT 172	n/a	n/a	√	√	√	n/a
Degree of dissolution	MT 179	n/a	√	n/a	√	n/a	n/a
Persistent foam	MT 47.2	√	√	√	√	√	n/a
Elevated temperature stability	MT 46.3	√	√	√	√	√	√

What affects the choice of formulation type?

- Phys/chem props of ai (or combinations of ai's)
- Efficacy needs e.g. built in adjuvant, solvent etc.
- Use pattern/applicn technology (e.g. spray drift)
- Environmental effects (e.g. Residues, leaching)
- Ease of use (Kg/Ha)
- Safe handling/Hazard classification
- Transport & storage
- Cost
- Ease of Manufacture
- Prior art – Patents!

Thank you – questions?

- **BACK UP SLIDES**

Soluble Granule (SG)

Description:

Solid granule formulation which dissolves on addition to water for spray application

Advantages

- High active loading
- No tank residue
- Low dust (extrusion)
- Easy to package
- No flash point and reduced C+L

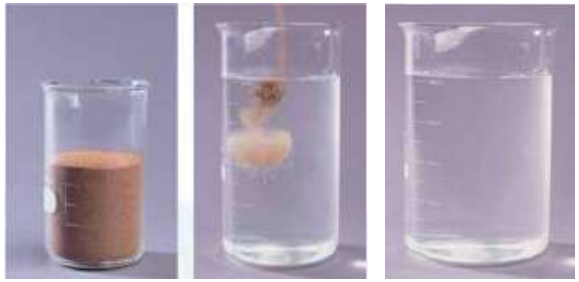
Disadvantages

- Can be expensive to manufacture - drying
- Slow dissolution in cold water can occur
- Dosing by farmer is difficult (density variations)

Soluble Granule (WG)

SG formulations are dissolved in water for application

On addition to water, the granules dissolve to give a suspension free homogenous solution of active ingredient



Extruded SG

Soluble Granule (SG)	
Component	**Typical Loading (g/Kg)**
Active ingredient salt	950
Impurities	Balance

Wettable Powder (WP)

Description:

Solid powder formulation for dilution in water

Advantages

- Easy to manufacture
- High active loadings possible
- Low cost (except with PVA packaging)
- No flash point (no solvent)
- Existing technology

Disadvantages

- Dustiness (inhalation issue)
- Poor wetting or dispersion in water
- Poor tank mix compatibility with other products
- Dosing by farmer is difficult (low use rates)
- Poor pack rinsing (unless in sachet)

Concentrated Oil-in-Water Emulsions (EW)

Description:

Multiphase formulation where the active ingredient (dissolved in solvent) is emulsified into water producing opaque liquid (droplet size 0.1 – 10µm)

Advantages

- Aqueous based system
- Lower organic solvent content
- Higher or no flash point
- Reduced potential for phytotoxicity
- Allows combination of water and oil soluble actives

Disadvantages

- Low active content
- Higher complexity development
- More complex manufacturing process
- Higher sensitivity to storage conditions

Microemulsion (ME)

Description:

Multiphase formulation where the active ingredient (dissolved in solvent) is emulsified into water producing clear solution (droplet size ~10nm)

Advantages

- Easy to manufacture
- Very stable at all dilution rates
- Aqueous based
- Higher or no flash point
- Translucent / clear

Disadvantages

- Low active content
- Higher surfactant may lead to foaming issues
- Expensive raw material costs

Macro versus Micro Emulsions

Macro emulsions have emulsion droplet size >0.1µm and are typically white (due to refraction of light)

Component	Typical Loading (g/L)
Active ingredient	25 - 600
Solvent	0 - 250
Emulsifiers	20 - 60
Antifreeze	0 - 100
Antifoam	1 - 2
Biocide	0 - 2
Rheology aid (gels)	1 - 20
Water	Balance

Micro emulsion droplet size is around 0.1nm and are typically clear

Component	Typical Loading (g/L)
Active ingredient	20 - 400
Surfactant	5 - 300
Co-surfactant / co-solvent	2 -200
Solvent	5 - 250
Water	Balance

Capsule Suspensions (CS)

Description:

Multiphase formulation whereby active ingredient is contained within a capsule and suspended in water

Advantages

- Allows controlled release
- Can adapt release profile of active
- Reduced toxicity
- No or low solvent content
- Allows solid formulation of liquid active
- Can solve difficult to formulate concepts

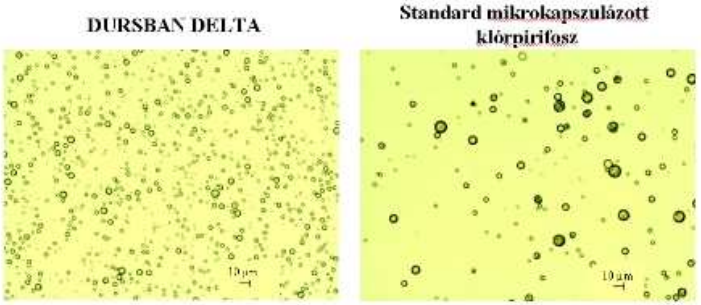
Disadvantages

- Complex technology with long development time
- Expensive and complex to manufacture
- Physical instability on storage (settling, syneresis)
- Lower active ingredient content

Capsule Suspension (CS)

CS formulation consist of physical walled capsules containing the liquid active ingredient for dilution in water

Component	Typical Loading (g/L)
Active ingredient	upto 400
Emulsifiers	10 - 50
Dispersing agent	20 -50
Antifreeze	50 - 100
Antifoam	1 -2
Biocide	1 -2
Rheology aids	1 - 5
Solvent	0 - 200
Water	Balance



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