June, 2010

Bioabsorbable Polymer

Poly(DL-Lactide-co-Glycolide)

Mitsui PLGA Series

Mitsui Chemicals

What is Mitsui PLGA?

USES

PLGA is a unique base polymer for controlled release of drugs and medical implant materials.

PROPERTIES

Standard grade of PLGA is an almost colorless or light tan solid manufactured in transparent pellet form.

PLGA is easily decomposed into glycolic acid and lactic acid by reaction with water.

Each grade of PLGA has a different rate of decomposition process.

Advantage of Mitsui PLGA for Medical Use

- Least Residual Solvent
- Molecular Weight is well Controlled
- Drug Master File is registered with FDA
- Manufactured under cGMP

APPLICATIONS (*Examples 1)*

Anti-Cancer Drug

US 5304377

•Microcapsule of Leuprorelin acetate with PLGA and PLA

Control of releasing time of the drug → Prolong the anti-cancer effect

US 5603961

•Microsphere of CDPP (Cisplatin) with PLGA and PLA

Control of initial burst and releasing time of the drug → Lower the toxicity and stabilize the anti-cancer effect

APPLICATIONS (*Examples 2)*

GnRH analogues for prostate cancer

ZOLADEX(AstraZeneca)

•Pellet of Goserelin acetate with PLGA

Control of releasing time of the drug
(interval：28days，12weeks）

→ Prolong the anti-cancer effect

DECAPEPTYL(Debiopharm)

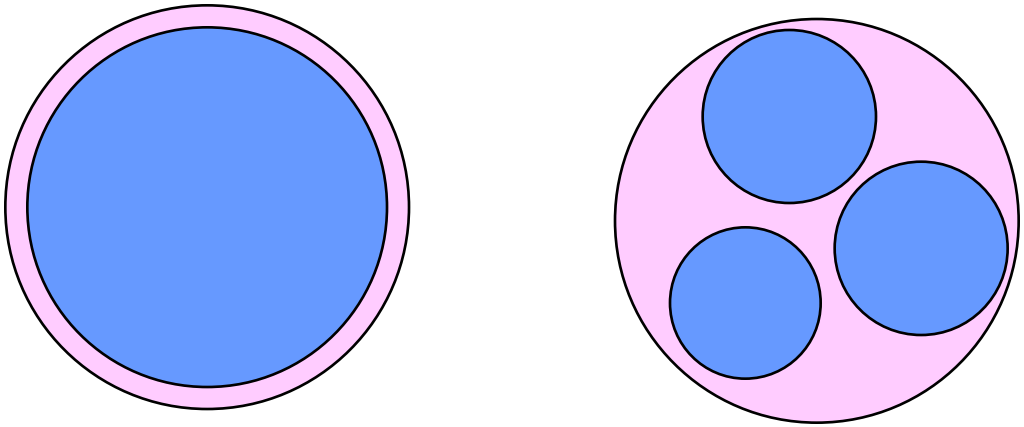
•Microsphere of triptorelin with PLGA and PLA

Control of initial burst
and releasing time of the drug
(interval：1week～6months）

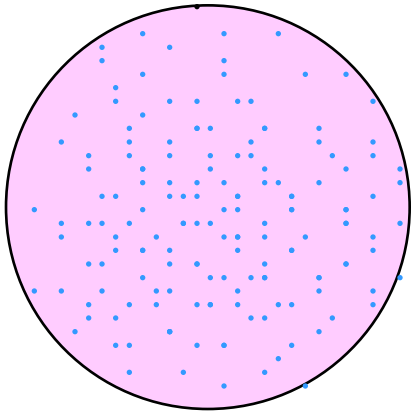
→ Prolong the anti-cancer effect

Structures of Release Controlled Drugs

- Microcapsule



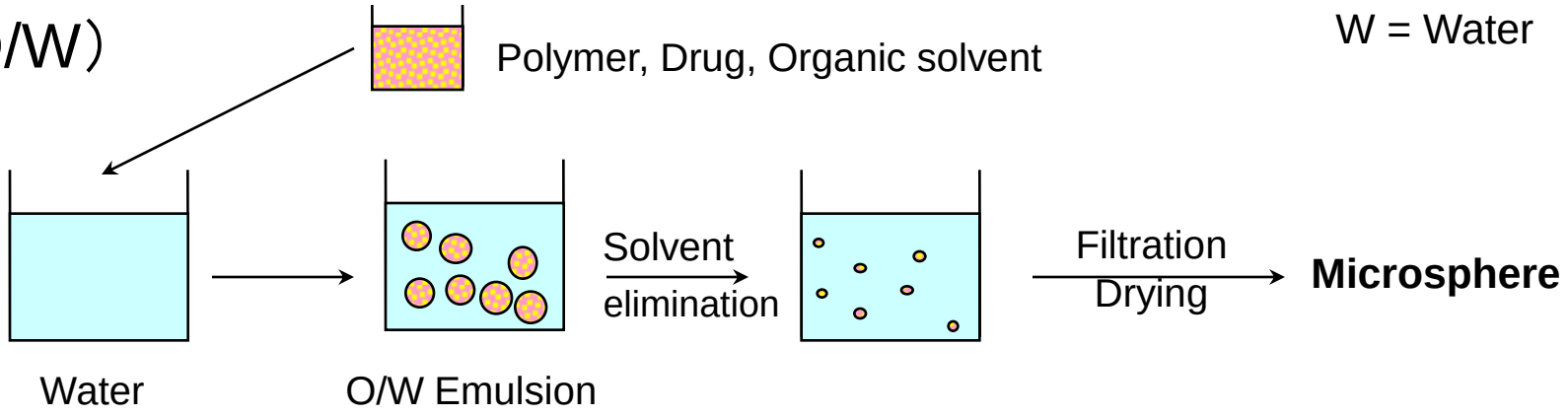
- Microsphere



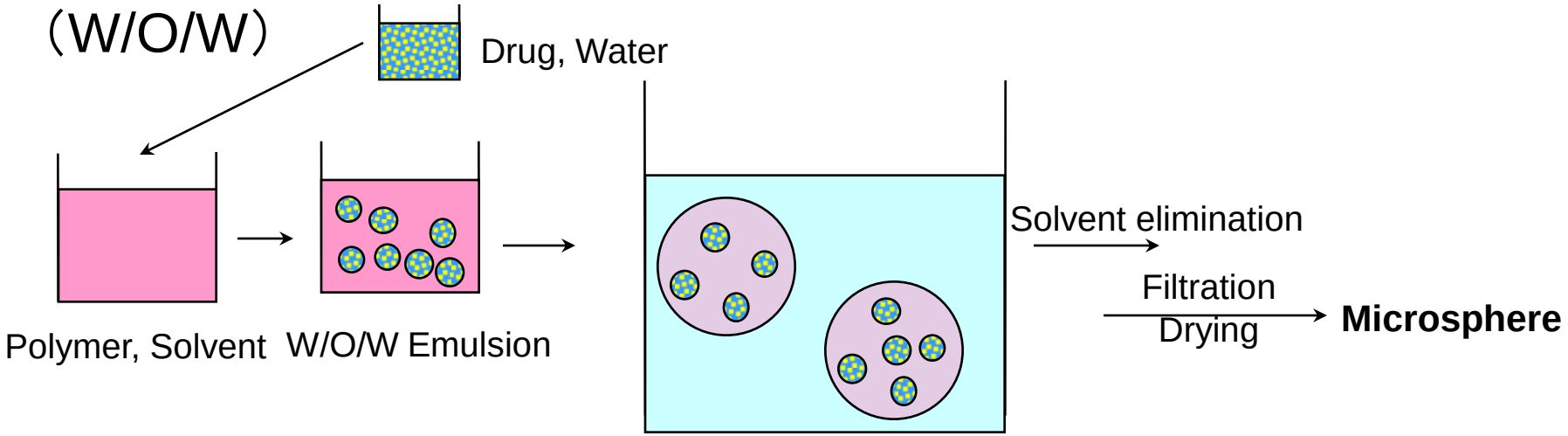
Formulation (1)

- Emulsion
  （O/W）

O = Oil
W = Water

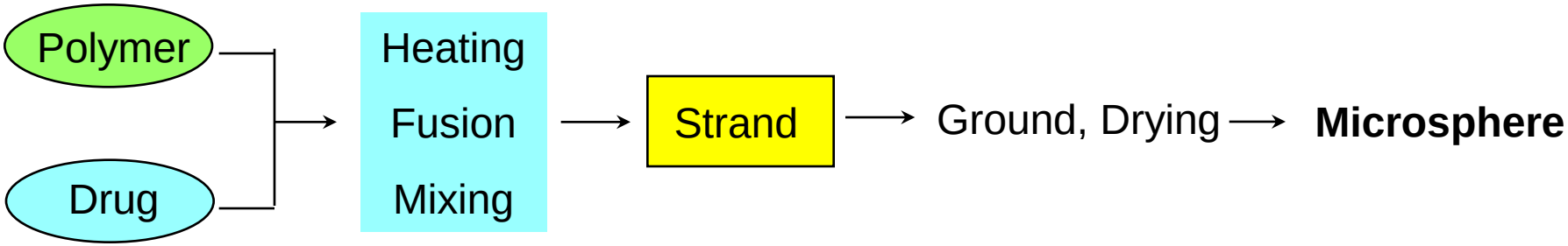


（W/O/W）

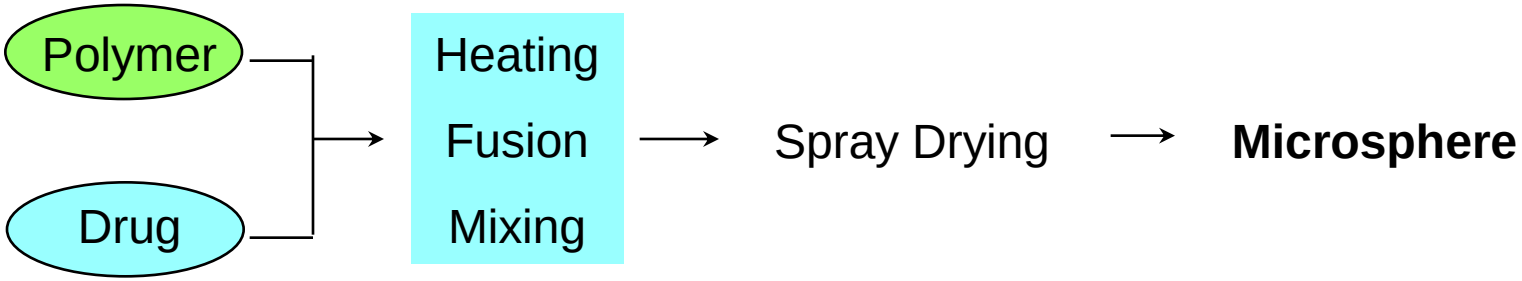


Formulation (2)

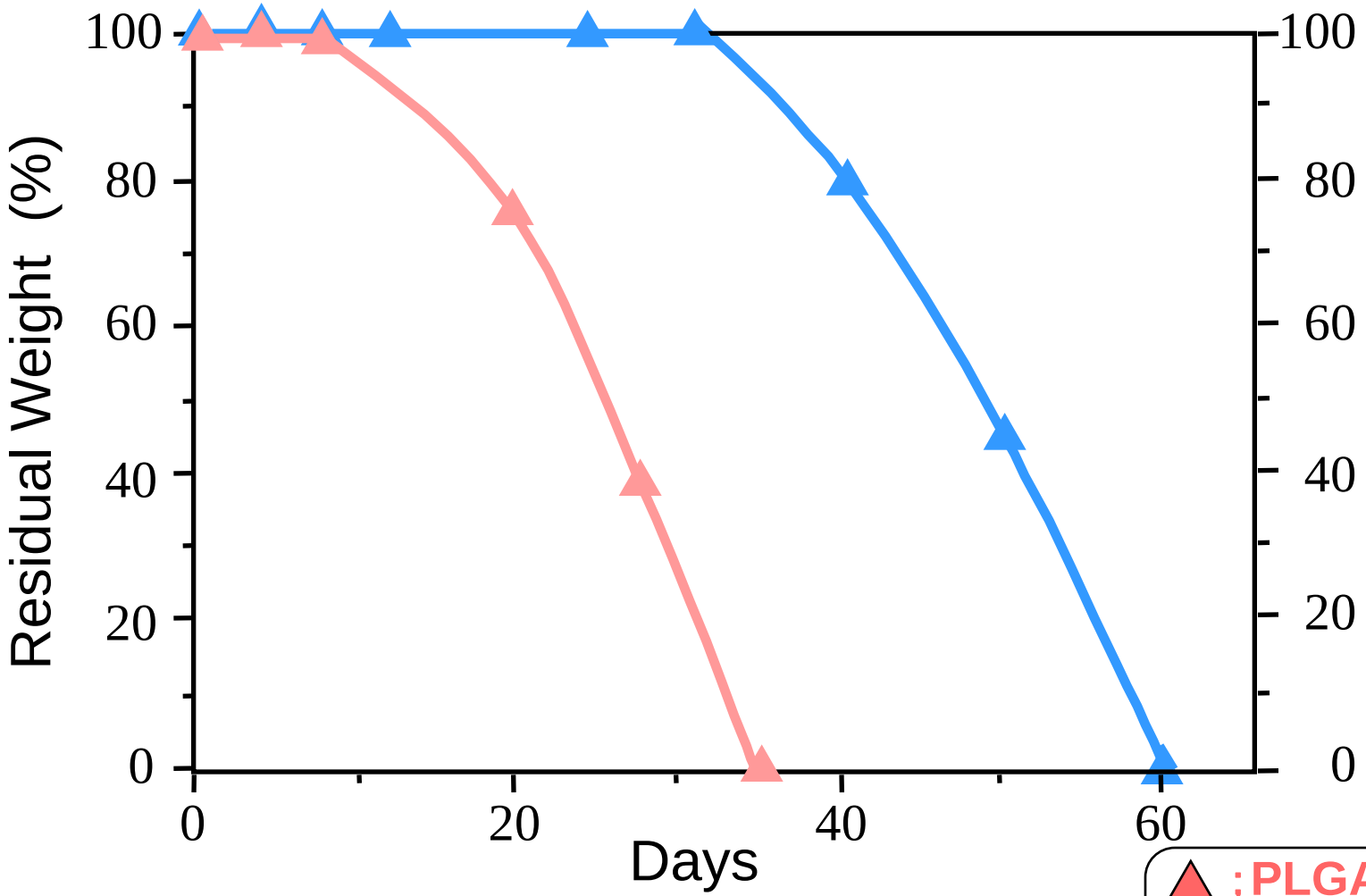
- Fusion



- Spray dry



Hydrolysis of PLGA in vitro (Residual Weight)



Hydrolysis conditions
in phosphate buffer solution (pH = 7.3) temp: 37 ℃

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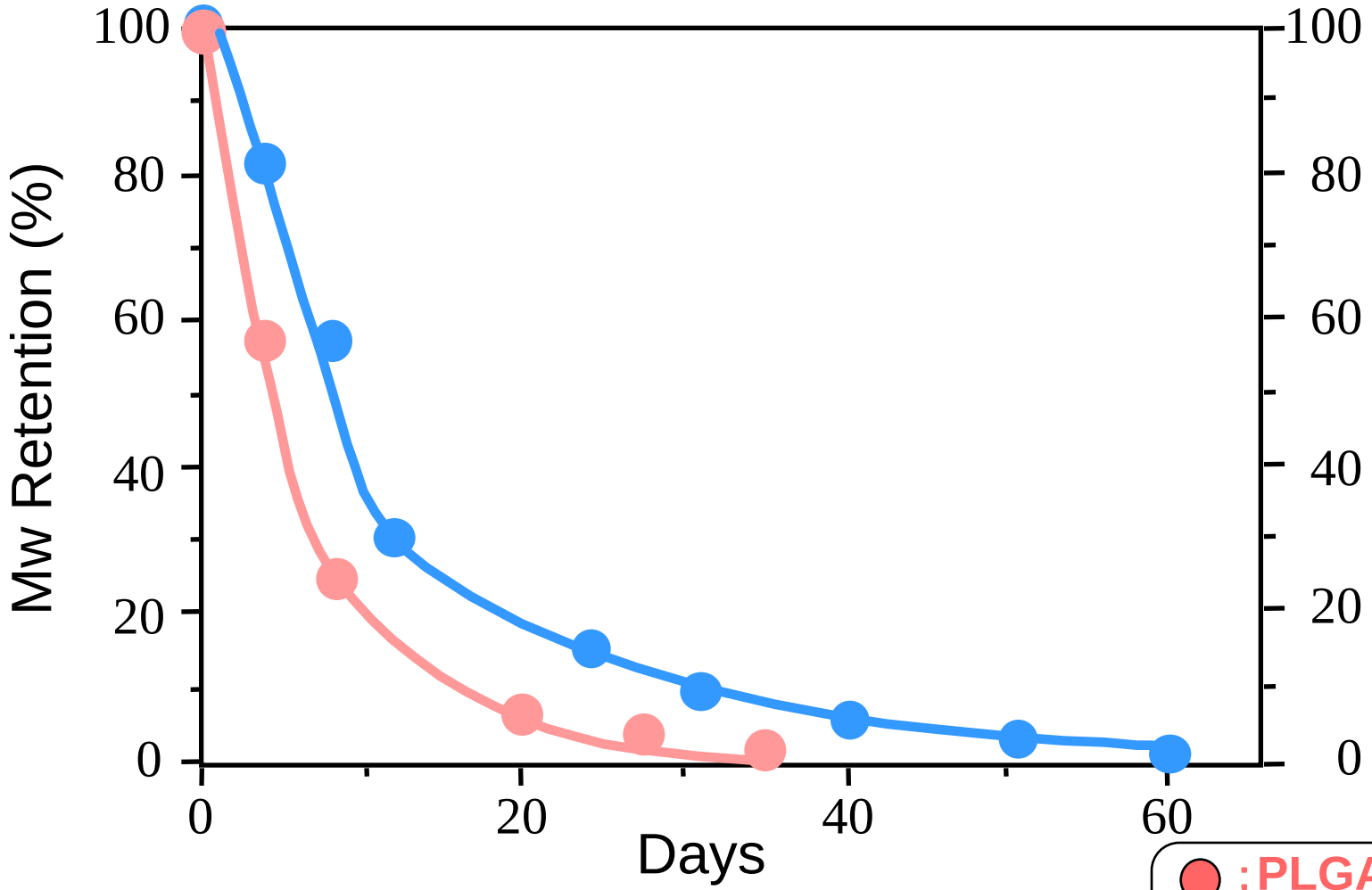
Hydrolysis of PLGA in vitro (Molecular Weight)



Hydrolysis conditions
in phosphate buffer solution (pH = 7.3) temp: 37 ℃

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Physical Properties

	PGA	PLGA 5	PLGA 75
CAS No.	26202-08-4	26780-50-7	
Chemical Formula	$(C_4H_4O_4)_x$	$(C_4H_4O_4)_x (C_6H_8O_4)_y$	
Color	light tan	white to light tan	
Odor	Odorless	Odorless	
Tm（Melting Point）／ºC	220-230	—	
Tg（Glass Transition）／ ºC	35-40	45-55	
Solubility	HFIP	CH_2Cl_2 $CHCl_3$ DMF DMSO THF	

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Properties

Polymer	Co-polymer ratio, mol%		*Inherent Viscosity	**Molecular Weight	Residual monomer, %		Sn content	Heavy metals	Sulphated ash
	GLD	LTD(form)	dL/g	kDa	GLD	LTD	ppm	ppm	%
PGA	100	–	0.90 – 1.10	(100)	< 1.0	–	< 10	< 10	< 0.1
PLGA 5-50	45 – 55	45 – 55(DL)	0.45 – 0.60	(50 – 55)	< 2.0	< 2.0	< 50	< 10	< 0.1
PLGA 75-75	20 – 30	70 – 80(DL)	0.72 – 0.80	(78 – 85)	< 2.0	< 2.0	< 50	< 10	< 0.1
PLGA 75-65			0.60 – 0.70	(62 – 76)					
PLGA 75-50			0.45 – 0.55	(50 – 60)					

*Inherent viscosity : PGA : 0.5 g /dl (2, 4, 6-Trichlorophenol / Phenol = 7 / 10), 30℃,
PLGA 5, PLGA 75: 0.5 g / dl (Chloroform), 25℃

**Molecular Weight (by GPC) : (Standard polymer-Solvent)
PMMA-HFIP for PGA, PS-THF for PLGA

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GRADE

Standard grade “PLGA 5-50” is a product with the decomposition rate of one month, and “PLGA 75-65” is a product decomposing in three months.

“PLGA 75-50”, “PLGA 75-65” and “PLGA75-75” which decompose slower than “PLGA 5-50”. Upon request, the products of which physical properties and inherent viscosity are partially altered, are available as a special grade.

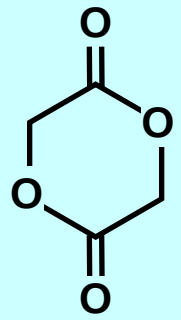
One of the characteristics of our PLGA is that no solvent remaining in this product. This is due to our unique manufacturing method which does not contain solvent in the manufacturing and purifying processes.

GMP & DMF

The PLGA series are manufactured at our cGMP plant in Nagoya Works .

Drug Master File is filed to FDA and Medicine Control Agency of U.K., Product Master File is filed to Canadian Authority in 5 and 75 type respectively.

Ring Opening Polymerization of Glycolide and (or) Lactide



Glycolide (GLD)

Catalyst
Initiator

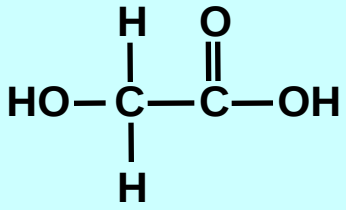
PGA

[CAS No. 26202-08-4]

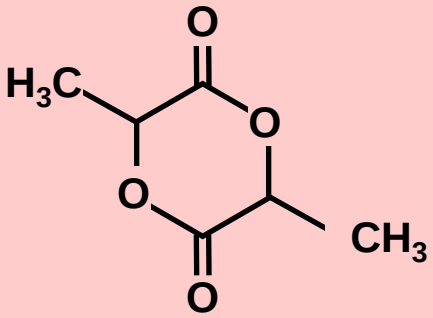
PLGA

[CAS No. 2678050-7]

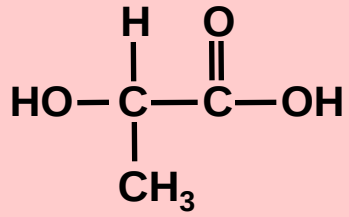
Hydrolysis



Glycolic Acid



Lactide (LTD)



Lactic Acid

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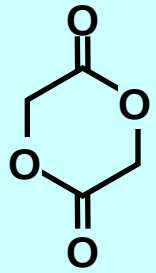
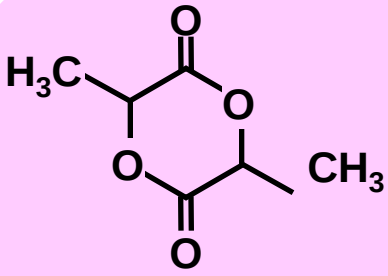
Manufacturing Process of PLGA



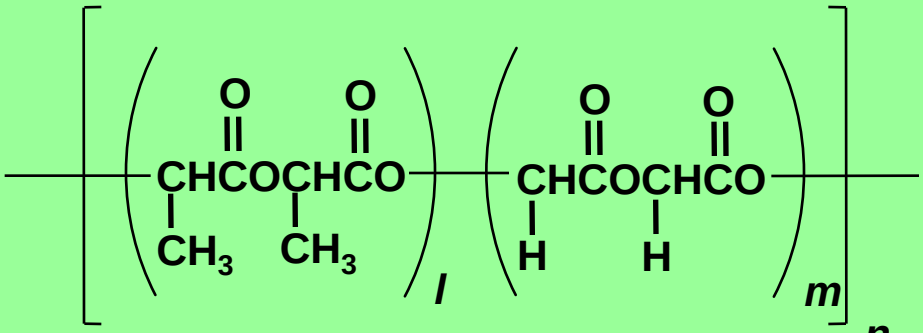
GLD



LTD

Catalyst
Initiator

Polymerization → **Removal of Monomers** → **Pelletization or Crashing**



PLGA

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