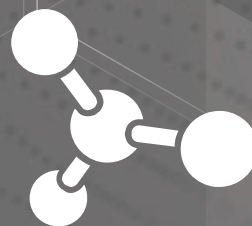


Executive Summary



YUHAN
CDMO



Full-spectrum Service



Early stage

Late stage

Commercial

Process Development

- Synthetic route scouting
- A broad range of scale-up
- Polymorph study

- Process optimization & Crystallization study
- Safety & Hazard assessment
- Process simulation
- Control strategy
 - PAR study, DoE study

- Technical transfer
- Process Validation
- Back integration

Analytical Development

- Analytical method development
- Impurity identification

- Standard Characterization
- Trace analysis (GTI) & impurity profiling
- Forced degradation study
- Method Validation/Transfer

- Analytical support

Manufacturing

- non-GMP (60~150L reactors)
- cGMP pilot (100L~)
- Strong R&D support tech transfer

- cGMP manufacturing (Typical batch size: 10kg~)







- cGMP manufacturing (Total capacity: 700m³)
- Continuous improvement

Project Management

Single Point of Contact

Executive Summary

Regulatory / Compliance

cGMP Plants	Regulatory Agencies		
Ansan	 Korea	10 times 1999-2023	MFDS
	 US	10 times 2002-2020	FDA
	 Australia	4 times 2004-2012	TGA
	 Japan	6 times 2006-2020	PMDA
Hwaseong	 Korea	3 times 2016-2022	MFDS
	 US	2 times 2017-2018	FDA

PSCI / SCM

- Top CDMO initiative for continuous improvement
- Trusted Supplier to many of PSCI member companies
- No delay during COVID-19
- RM supply risk assessment
- RM Nitrosamine risk control

Geo-Political Status

- Tariff Exemption (EU/US+a FTA)
- Zero logistics interruption
- More than 10,000 foreign entities in business in Korea
- No major conflict with North Korea since Korean war in 1953
- Frequent visits from customers

Contents

- Compliance
 - PSCI / SCM
 - Geo-Political Status
-
- Work Culture
 - Experienced
 - Lead Time
 - Data Integrity
-
- EH&S
 - Contingency
 - Potent Compound
 - Various Options

Executive Summary

Work Culture

- Nimble & Agile
- PATT Culture
 - ✓ Proactive
 - ✓ Accountable
 - ✓ Transparent
 - ✓ with Technical Excellence

Experienced CDMO

- CDMO Business since 1980
- Collaboration with 30+ customers
 - ✓ Small to Mid-size biotech
 - ✓ Global Big Pharma (Top 10)
- 200+ Chemistry Reactions
- Average 10+ years Experience
- on-site Tech Transfer (R&D to GMP)

Lead Time

- Project Initiation:
 - ✓ 2 weeks upon PO
- Manufacturing:
 - ✓ 3~4 months in general (RM)
 - ✓ Flexible manufacturing slot

Data Integrity

- Back-up storage in 3 data centers
- 21 CFR Part 11 Compliance
 - ✓ TrackWise, Veeva
 - ✓ Compliance Wire
 - ✓ Empower 3
 - ✓ NuGenesis
 - ✓ LabX & more

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Executive Summary

EH&S

- Routine EH&S Audits
- K-REACH Compliance
- Dedicated EH&S Team
- Process Safety Evaluation
- Hazard Review
- Thermal Hazard Screening
- Process Risk Assessment

Contingency

- Two separate cGMP Sites
- Disaster contingency

Potent Compound

- Potent Compound handling
- CPT $1\mu\text{g}/\text{m}^3$ (Safe Bridge[®] OEL 3A)
 - ✓ Pilot to Commercial Scale

Various Manufacturing Options

- High Pressure Hydrogenation Reactor
 - ✓ Pilot: ~50 bar / Commercial: ~10 bar
- Cryogenic Reaction down to -80°C
- Micronization / Milling Options
 - ✓ Wet Mill, Air Jet Mill, Fitz Mill, Conical Mill
- Wide Reactor Size Range: 100L ~ 12,000L
- Total Reactor Volume: 700m^3

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List of Chemical Transformations

Chemical Reaction (Transformation)	Example	Reactants		Reagent	Scale
Cross Coupling	Sonogashira coupling	Aryl bromide	Alkyne	Pd(PPh ₃) ₂ Cl ₂	150 kg
		Aryl bromide	TMS-acetylene	Pd(PPh ₃) ₄ , CuI	350 kg
	Suzuki coupling	Aryl iodide	Aryl boronate	PdCl ₂	260 kg
		Aryl iodide	Aryl boronic acid	Pd(OAc) ₂ , NaOH	125 kg
		Aryl chloride	Alkyl borate	PdCl ₂ (amphos) ₂ , 2-MeTHF, NaHCO ₃	105 kg
	Buchwald-Hartwig amination	Arylbromide	carbamate	Pd(Oac) ₂ , Xantphos, K ₂ CO ₃	270 kg
	Grignard reaction	Piperidinone		ArMgBr	450 kg
		Epichlorohydrin	alkylMgCl	THF	240 kg 260 kg
	Grignard reaction / carboxylation	Aryl bromide		i-PrMgCl / CO ₂	20 kg
	Metalation / ring opening	Bromopyridine	Aziridine	1) Turbo Grignard (i-PrMgCl·LiCl), 2) CuI	15 kg 70 kg
	Metalation / formylation	Bromopyridine	DMF	i-PrMgCl, n-BuLi	25 kg
	C-H borylation for Suzuki coupling	N-alkyl pyrazole		n-BuLi, i-ProB(Pin),	150 kg
Aryl bromide			Pd(PPh ₃) ₂ Cl ₂ , B ₂ Pin ₂ , EtCO ₂ K	150 kg	
Amide bond formation	Coupling of carboxylic acid with amine	Carboxylic acid	Primary amine	PPACA (T3P), Et ₃ N	250 kg
		Carboxylic acid	Secondary amine	DMF, (COC ₂) ₂ , K ₂ CO ₃	10 kg
		s	Cyclic amine	HBTU, EIPEA	10 kg
		Carboxylic acid	Primary amine	CDI	20 kg
		Carboxylic acid	Primary amine	DPP-Cl, TEA	10 kg
	Weinreb amide	Carboxylic acid	N,O-Dimethylhydroxylamine	EDC HCl, DIPEA, HOBT, DCM	200 kg
	Amidation of ester	Ester	N ₂ H ₄ · H ₂ O		300 kg
C-N coupling	Mannich reaction	secondary amine, formaldehyde,	α-methylene carbonyl	AcOH	150 kg
	Coupling	Amine (secondary)	Carbamate	TEA	15 kg

List of Chemical Transformations

Chemical Reaction (Transformation)	Example	Reactants		Reagent	Scale
Alkylation	N-alkylation	Bis-silyl compound	benzyl chloride	KI	80 kg
		Pyrazole	Alkylbromide	Water, TBAB, NaOH	90 kg
		Hydrazine	Bromoacetate, isocyanate	TEA, MeOH	100 kg
		N-Sulfinyl amine	MeI	KOH	20 kg
	O-alkylation	Phenol derivative	alkyl chloride	NaHCO ₃ , NaI, NMP	100 kg
		Chloroisoquinoline	NaOMe	MeOH	25 kg
	Mitsunobu reaction	Alcohol	Aryl alcohol	DIAD, PPh ₃	10 kg
	Horner-Emmons Wittig reaction	Ketone	phosphonate	KOH	50 kg 100 kg
Alkoxycarbonylation	alkyl pyridine	Dimethyl carbonate	NaHMDS	20 kg	
Hydrogenation	Debenzylation & alkene reduction	benzyl protected unsaturated ester		Pd(OH) ₂ , AcOH, H ₂	50 kg 100 kg
	Reduction	pyridine		Pt/C, H ₂	NA
	Debenzylation	Benzylpiperidine		Pd/C & H ₂	300 kg
	Debenzylation	N-benzyl amine (tertiary)		Pd/C, H ₂ (gas), TFA	5 kg
	Nitro reduction	Aryl Nitro		Pt/V & H ₂	260 kg
	Cbz deprotection	Cbz protected amine		H ₂ , Pd/C	60 kg
Oxidation	Albright-Goldman oxidation	Secondary alcohol		DMSO / Ac ₂ O	80 kg
	TEMPO/Bleach Oxidation	Secondary alcohol		NaOCl, TEMPO, MTBE	200 kg
	α-Hydroxy ketalation (PIDA oxidation)	Cyclic ketone		PIDA((diacetoxyiodo)benzene)	100 kg
	Dehydrogenation with DDQ	Dihydropyridinone		DDQ	25 kg
Reduction	Ester reduction to alcohol	Ester		NaBH ₄ , CsCl ₃ · 7H ₂ O	20 kg
	Weinreb amide reduction)	Weinreb amide		LiAlH ₄ , THF	70 kg

List of Chemical Transformations

Chemical Reaction (Transformation)	Example	Reactants		Reagent	Scale
Reductive amination	Condensation of ketone and sulfinamide, followed by reduction	Ketone	Ellman's sulfinamides	Titanium alkoxide, NaBH ₄	30 kg
	Condensation of ketone and amine, followed by reduction	Ketone	chiral amine	Titanium alkoxide, NaBH ₄	10 kg
	Reductive amination	Secondary amine	Formaldehyde (37%)	STAB (Sodium triacetoxyborohydride), AcOH	10 kg
Esterification	Esterification	carboxylic acid		SOCl ₂ , MeOH	NA
		Glyoxylic acid	L-Menthol	H ₂ SO ₄ , toluene	1,100 kg 1,000 kg
Halogenation	Chlorination	Aryl chloride		NH ₄ OH	200 kg
		Isoquinolinone		POCl ₃ , TEA	30 kg
	Chlorination	Primary alcohol		SOCl ₂ , DCM, NaHCO ₃	120 kg
	Bromination	Pridine		NBS	100 kg
Fluorination	Oxidative de-sulfurization fluorination	Thioketal		DBDMS, HF-Pyridine, DCM	130 kg 130 kg
	Electrophilic fluorination	Benzylic CH ₂		N-fluorobenzenesulfonimide (NFSI), NaHMDS	120 kg
Cyclization	Oxadiazole synthesis	Acetohydrazide		CH(OCH ₃) ₃	170 kg
	Cyclization	hydrazide		TsCl, K ₂ CO ₃	15 kg
	Cyclization	isothiocyanate	thioglycolate	DIPEA	130 kg
	Pyrazole ring formation	a-b-unsaturated ketone	alkyl hydrazine	AcCl, EtOH, LiCl	200 kg
	Lactone formation (Lactonization)	L-Methionine		Bromoacetic acid, IPA, H ₂ O, AcOH	15 kg
	Thiazole ring formation	Thioamide	dichloroacetone	Acetone	15 kg
Condensation	Knoevenagel condensation	Aldehyde	thioxazolidinone	-	200 kg
	Claisen condensation	Ketone	Ester	LiHMDS, MeTHF	450 kg
Oxime formation	Oxime formation of a-carbon of ketone	Cyclic ketone		^t Bu-ONO, KO ^t Bu, MTBE	100 kg
	Oxime formation of a-b-unsaturated ketone	a-b-unsaturated ketone		NaNO ₂ , H ₃ PO ₄ , H ₂ O	250 kg

List of Chemical Transformations

Chemical Reaction (Transformation)	Example	Reactants		Reagent	Scale	
Formylation	Formylation and cyclization	Ethyl fluoroacetate	Aldehyde	NaOMe, Urea	280 kg	
	Formylation	Protected hydroxybenzene	DMF	n-BuLi	350 kg	
Epoxidation	Epoxidation	Halohydrin		KOH, MTBE	250 kg	
Bisulfite adduct formation	Bisulfite adduct formation	Menthyl ester		Aq. NaHSO ₃	1,100 kg 1,000 kg	
Thioamide formation	Thioamide formation	Amide		P ₂ O ₅ , THF, Na ₂ CO ₃	10 kg	
Hydrolysis	Hydrolysis of Ester	Ester		Aq. KOH, EtOH	150 kg	
				KOH	100 kg	
		Aq. NaOH	100 kg			
	Hydrolysis of Oxime	Ketoxime		TsOH, MEK/H ₂ O	250 kg	
Protection	Acetalization	Aldehyde		EtOH, 4M HCl in dioxane	70 kg	
	Mesylation-demesylation	Primary amine		MsCl, Et ₃ N, Na ₂ CO ₃	100 kg 200 kg	
	Silylation	Alcohol	TBDPSCI	Imidazole	25 kg	
	Silylation	Hydroxypyridinone		HMDS, (NH ₄) ₂ SO ₄	80 kg	
	Acetalization	Aldehyde		EtOH, 4M HCl in dioxane	70 kg	
	Thioketalation	Ketone		EDT (1,2-Ethanedithiol), TsOH, AcOH	250 kg	
	Tritylation	Alcohol	Trityl chloride		DBU, DCM	300 kg
	Mixed acetal	Aryl alcohol	Ethylvinyl ether		PPTS, THF	320 kg
	Boc-protection	N-tosyl amine			Boc anhydride	15 kg 70 kg
	Deprotection	Desulfinylation	N-Sulfinyl amine (tertiary)		Methanolic-HCl	10 kg
Desilylation		Silyl ether		TBAF	10 kg	
Boc deprotection		Boc protected amine		HCl	10 kg	



Thank you

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