

**Full-service CRO** 

**GLP** Certified



www.dtncro.com

# History

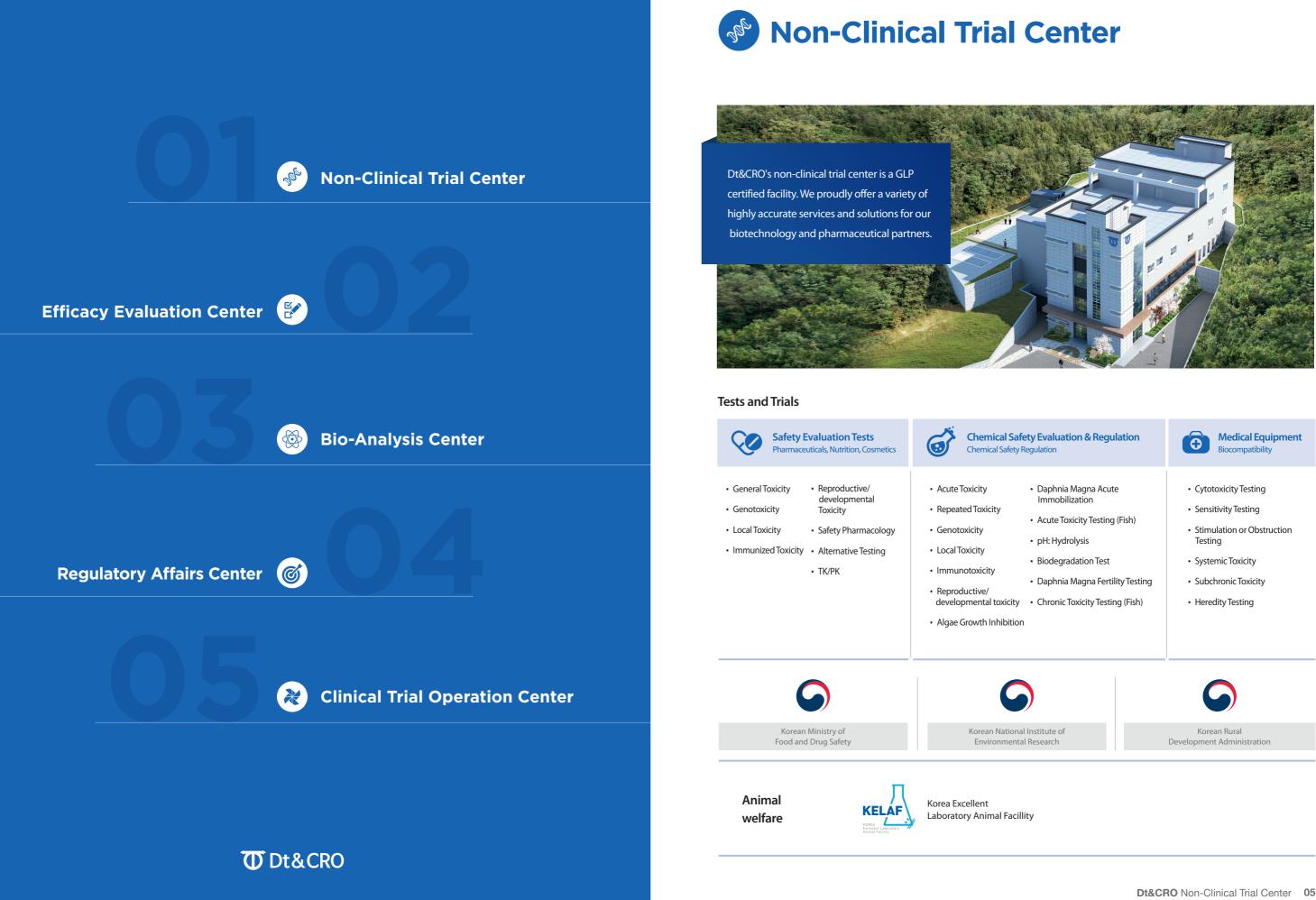
## Our creativity and passion drives our dream of **Becoming the future of CRO.**



### **Dt&CRO**

•	Clinical trial training contract with Korea University Medical Center
•	MOU with AVANCE CLINICAL
•	Construction of PK/PD center begins
•	Efficacy evaluation center expansion and transfer
•	KOSDAQ Listed
•	Operation of Smart Clinical Center (STC)
•	Completion of Efficacy Evaluation Center
•	First local entity to introduce Triple Quad 7500 analysis equipment
•	Merger and Acquisition of EBO Co., Ltd., an efficacy evaluation provider
•	Veterinary drug GLP service commences
•	Non-clinical trial SEND service (for submission to the US FDA) commences
•	Medical Device GLP testing services commence
•	Chemical and Pesticide GLP testing services commence
•	Pharmaceutical GLP testing services commence
•	Non-clinical trial center established
•	Test schedule management program (MoPS) released
•	Recognized as an affiliated research institute
	Designated as a bioequivalence testing agency
	Protein characterization service commences
•	Biopharmaceutical and biological sample analysis center established
•	Clinical-trial service commences

Dt&CRO Corp. established



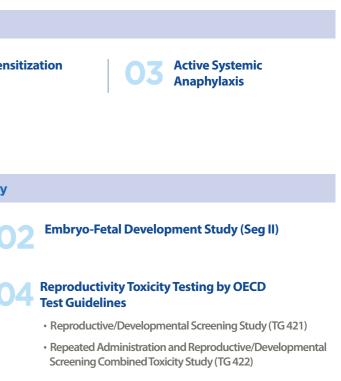
## Dt&CRO | Non-Clinical Trial Center

# **Safety Studies**

General Toxicity Study			Immunotoxicity Study	
Ol Single Dose Toxicity Study	02 Repeated Dose Toxicity Study	03 Tumorigenicity Study		Photosen: Test
			Passive Cutaneous Anaphylaxis	
Genotoxicity Study			Reproductive and Developmental Toxicity	y Study
O1 AMES Test	02 In Vitro Chromosomal Aberration Test	03 In Vivo Micronucleus Test	Fertility and Early Embryonic Development Study (Seg I)	0
04 Mouse Lymphoma Assay	05 Comet Assay	06 In Vitro Micronucleus Test	O3 Pre-and Postnatal Development Including Maternal Function Study(Seg III)	0
Local Toxicity Study				
<b>Skin Irritation Test</b>	O2 Cumulative Skin Irritation Test	<b>63</b> Eye Irritation Test	Safety Pharmacology	
	Irritation lest		Core Battery · Central Nervous Sys Study · Central Nervous Sys	
Other related tests Oral mu	cosal Irritation Test Local Tolerance Test	Vaginal, Rectal Mucosal Irritation Test	Respiratory System     Cardiovascular System	
			- Telemetry (In Vivo) - hERG assay (In Vitr	



## Dt&CRO | Non-Clinical Trial Center



# Pathology



Necropsy 01

**Clinical Pathology** 

#### 03 Histopathology

#### **Clinical Pathologic Examinations**

Hematology	Blood Chemistry	Urinalysis	Hormones
<ul> <li>XN-1000, Sysmex</li> <li>RBC, HGB, HCT, MCV, MCH, MCHC, PLT, RET, WBC, NEU, LYM, MONO, EOS, BASO, RDW, PDW, PCT, MPV</li> <li>CA 660, Sysmex</li> <li>PT, APTT, Fibrinogen</li> </ul>	▶ HITACHI 7180, Hitachi AST, ALT, ALP, GGT, T-BIL, T-CHO, TG, GLU, BUN, CREA, TP, ALB, IP, Ca, A/G Ratio, CK, LDH, HDL, LDL, TBA, Mg, UA, UREA, LIP, AMY, mTP, mALB, NEFA, GLDH, Na, K, CI	<ul> <li>UC-1000, Sysmex</li> <li>Urobilinogen, Blood, Ketone, Glucose, Protein, Bilirubin, pH, Nitrite, Leukocyte</li> <li>Sediment examination</li> <li>Cast, Epithelial cell, Leukocyte, Erythrocyte, etc.</li> <li>Visual examination</li> <li>Color, Specific gravity, etc.</li> </ul>	<ul> <li>ANYLAB F1, Z Bio T3, T4, TSH</li> <li>ELISA LH, FSH, Progesterone, Prolactin, Estradiol, etc.</li> </ul>

Histopathology Procedure

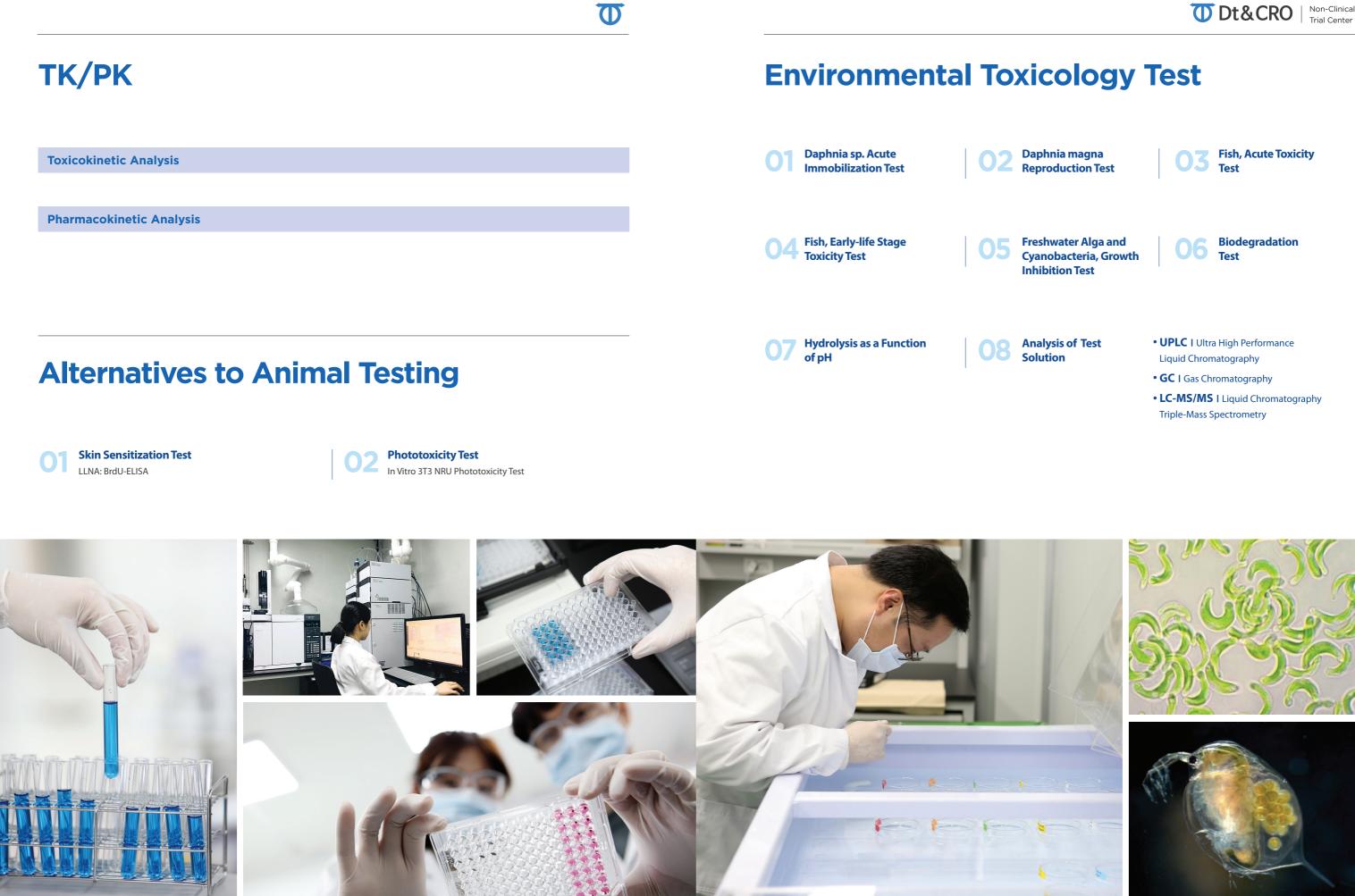
Procedures	Equipment / Solutions
Necropsy	Anesthesia(L-PAS-01, LMS)
Fixation	10% NBF, Davidson's sol.
Decalcification	10% Formic acid
Tissue processing / Embedding	Tissue processor(VIP6, Sakura)

Histopathology Examinations

Necropsy	Preparation (Paraffin)	Stain	Histopathology
Rodent • Rat • Mouse	<ul> <li>Tissue Trimming</li> <li>Tissue Processing</li> <li>Tissue Embedding</li> <li>Tissue Sectioning</li> </ul>	• Hematoxylin & Eosin	<ul> <li>Microscopic examination</li> <li>Peer review</li> </ul>
Non-Rodent <ul> <li>Rabbit</li> </ul>		Special Stain	Digital Pathology
• Beagle	e	<ul> <li>Masson's trichrome</li> <li>PAS(Periodic acid-Schiff)</li> <li>Gomori's chromaffin</li> <li>Oil Red O <ul> <li>Alcian blue</li> <li>Prussian blue</li> <li>Safranin O</li> <li>Toluidine blue</li> <li>Etc.</li> </ul> </li> </ul>	• WSI (Whole Slide Image) • Image analysis
	Frozen Section	IHC / IF Stain	



Procedures	Equipment / Solutions
Sectioning	Microtome Rotary(RM2245, Leica) Microtome slide(HM450, Epredia)
Staining / Mounting	Prisma <sup>™</sup> Glas <sup>™</sup> g2 (Sakura)
Microscopic observation	Light microscope(BX43, Olympus) Pannoramic 25 Flash III(3D Histech)



# **Efficacy Evaluation Center**

#### Drug efficacy evaluation test and biodistribution test



Conducting evaluation tests using cells or disease models for natural products, compounds, proteins, cell, and genes





Anti-cancer test

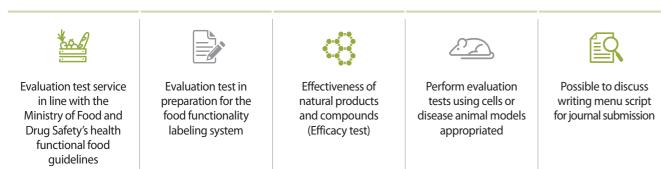
skin xenograft, orthotopic xenograft

**Biodistribution test** 

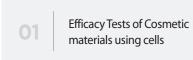
Perform biodistribution test for cell therapy products, gene therapy products, etc. (real-time PCR method)

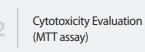


#### Efficacy evaluation test for Health functional food



### **Efficacy evaluation test for Cosmetics**





Whitening, Wrinkle improvement, Skin 03 elasticity, Moisturizing, Hair growth test

#### **Efficacy evaluation test items**

Category	Disorder	
-	Memory, Congnitive ability	Scopolamine-
	Parkinson's disease	• 6-OHDA-indu
-	Alzheimer's disease	<ul> <li>Amyloid-β-ind</li> </ul>
	Social deprivation	<ul> <li>Valproic acid-i</li> </ul>
Neurological Disease	Attention deficit hyperactivity disorder (ADHD)	• SHR model
	Relaxation	Stress-induced
	Sleep	<ul> <li>Caffein-induce</li> <li>Pentobarbital-</li> </ul>
-	Pain	Acetic acid, he
Retinal Disease	Retinal disorder	CNV-induced     NalO3-induced     MNU-induced     STZ-induced
	Dry eye syndrome	Tear gland inc
Gum Disease	Periodontitis	Ligation-induc
	Allergic rhinitis	• OVA-induced
	Expectorant	Quantification
Respiratory Disorder	Asthma	OVA-sensitizat
	Chronic obstructive pulmonary disease (COPD)	<ul> <li>LPS-induced r</li> <li>Elastase-induced</li> </ul>
	Pulmonary fibrosis	Bleomycin-inc
	Hypertension	• SHR Rat mode
Cardiovascular Disease	Blood clot, Blood flow	<ul> <li>FeCl3-induced</li> <li>Platelet aggre</li> <li>Blood coagula</li> </ul>
	Hepatitis	<ul> <li>Acetaminophe</li> <li>LPS, galactosa</li> </ul>
Liver Disease	Fatty liver	<ul> <li>Alcohol-induc</li> <li>High fat diet-induction</li> </ul>
-	Non-alcoholic steatohepatitis(NASH)	CDAHFD-indu     Western diet f
Gastrointes- tinal Disease	Gastritis	<ul> <li>Ethanol-induc</li> <li>Indomethacin</li> <li>Stress-induced</li> </ul>
	Constipation	<ul> <li>Loperamide-ir</li> </ul>
	Colitis	DSS-induced r
	Irritable bowel syndrome(IBS)	Acetic acid-inc

#### in vivo efficacy test method

e-induced impairment model

uced model(Stereotaxic injection)

nduced Alzheimer's disease model

-induced autism spectrum disorder model

ed model(water-immersion-restraint)

- ced sleet inhibition model
- al-induce sleep induction model

neat, formalin, surgery-induced model

- d wet-AMD model
- ed dry-AMD model
- d dry-AMD model
- diabetic retinopathy model
- cision model

uced model

l model

on using phenol red

ation-induced model

model ucde model

nduced model

lel

ed carotid artery occlusion model egation inhibition analysis lation analysis by PT and aPTT

hen-induced hepatic injury model samine-induced hepatic injury model

iced fatty liver model -induced NAFLD model

luced hepatic injury model

feeding model

iced model

in-induced model

ed model(water-Immersion-restraint)

-induced model

l model

nduced model

# **Bio-Analysis Center**

### **Efficacy evaluation test items**

Category	Disorder	in vivo efficacy test method
Prostate Disease	Prostatic hyperplasia	Testosteron-induced model
N I d	Chronic kidney disease (CKD)	Adenine-induced CKD animal model (oral or diet)
Nephropathy -	Gout	Hyperuricemia induction model by potassium oxonate
2	Osteoporosis	Ovariectomy-induced model
Bone	Kid's bone growth	Growth plate growth assessment, Maturity analysis
	Growth hormone evaluation	Pituitary Gland Ablation: A Model for Growth Inhibition
Hormone	Sexual maturity	
	<i>.</i> .	Dexamethasone-induced model
Muscle	Sarcopenia	• Aged model
Authoritie	Degenerative Osteoarthritis	MIA-induced model(intra-articular injuction)
Arthritis -	Rheumatoid Osteoarthritis	Collagen-induced model
	Obesity	HFD-induced model     ob/ob mouse
Metabolic Syndrome	Diabetes	<ul> <li>STZ-induced type I model</li> <li>db/db mouse type II model</li> </ul>
	Hypercholesterolemia	HCD-induced model
	Immunity enhancement	Cyclophosphamide (CYP)-induced model
Immunology and	Atopy	<ul> <li>DNCB-induced atopic dermatitis model</li> <li>Biostar (house dust mite)-induced model</li> </ul>
Inflammation	Psoriasis	Imiquimod (IMQ, aldara cream)induced model
	Allergenicity	IgE analysis using Brown Norway Rat
Skin wound	Wound	Cuts, burns, pressure sores-induced model
Fatigue	Fatigue improvement	Analysis using forced swimming and treadmill
Endurance	Endurance improvement	Analysis using forced swimming and treadmill
	Xenograft model	Tumor size measurement
Anticancer	Syngeneic model	Tumor size measurement
	Orthotopic model	Image analysis using IVIS
in vivo Distribution Assessment and Excretion	Stem cell, Tcell, Virus, Plasmid, Micro-organism	Analysis using real-time PCR in biological samples
Immuno-	Screening assay	
genecity	Confirmatiory assay	Antibody analysis using ELISA in body
(ADA), (nAb)	Titration assay	
PK, PD, Bio	maker analysis of Bio-drugs	ELISA, PCR, Flow cytometry
Others	Hangover cure	Blood test model after ethanol administration



Analyzed Products	
Small molecules (Synthetic, Natural)	
Polymer	
Biomarkers	
Proteins / Peptides	
Oligonecleotides (DNA, RNA, Aptamer)	

#### Non-GLP and Discovery Bioanalysis

 In-Vitro ADME (Plasma Protein Binding, Metabolic Stability, Metabolite Profiling & ID, Enzyme Inhibition)

Screening Pharmacokinetic Analysis

### GLP Bioanalysis

Dosing Formulation Analysis

Toxicokinetic Analysis

#### GCLP Bioanalysis

 Phamacokinetic Analysis Bioequivalence Analysis

### Biomarker Analysis

### Pharmaceutical Analysis

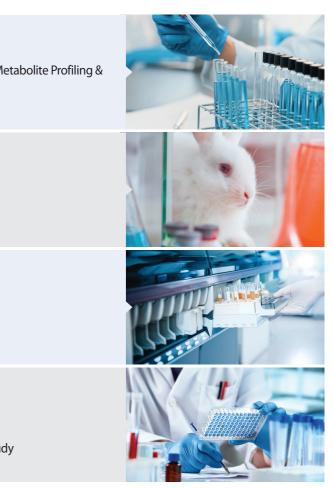
 Protein Characterization Purity / Impurity Test

 Impurity Identification Impurities Clearance Study

## **Dt&CRO** | Bio-Analysis Center

### Sample Matrices

#### Whole blood, Serum, Plasma, Urine, Feces, Tissue



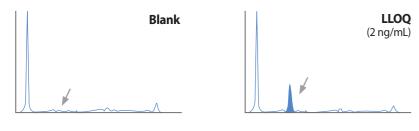
Equipment	
AB SCIEX API 5500, 6500 (X2), 7500 (X1)	Waters Xevo TQS, TQXS
AB SCIEX Triple Tof 5600+	Waters HPLC, UPLC with UV, RI detection
Molecular Devices Microplate Reader	

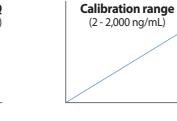
#### **Example of Test results for Problematic Analytes**

Semaglutide (2 ~ 2,000 ng/mL)

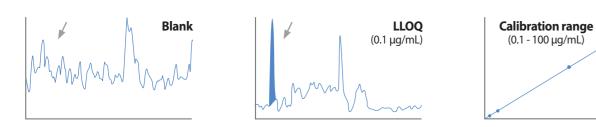
RNA (0.1 ~ 100 µg/mL)

Semaglutide





RNA





# Consulting service for MFDS/FDA

## **PM Consultation**

#### **Service Recipients**

• Companies entering non-clinical study phase for the purpose of applying for clinical studies

Companies experiencing challenges in deriving non-clinical study items

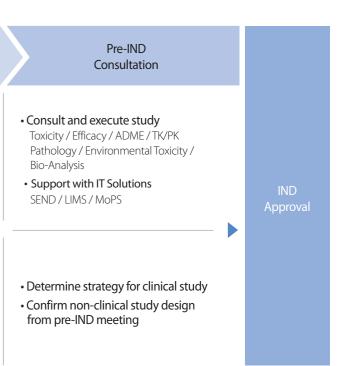
#### **Consultation Category**

- Review categorization of study drug / substance according to authorization
- Deduce non-clinical items by review of previously authorized cases
- Review check points for clinical study approval
- Consult non-clinical design for IND application such as MFDS and FDA

Service Procedure				
Request	Check Information	Review	Establish Strategy	Request Study
• Sponsor Request consultation	<ul> <li>Sponsor         <ul> <li>Clarify project intro- duction, Share drug / substance information</li> <li>Dt&amp;CRO                  Review project intro- duction and drug / substance information         </li> </ul> </li></ul>	Dt&CRO     Review study drug /     substance and     comparable cases	Dt&CRO     Provide information     on categorization     according to authori-     zation and procedures     → Propose non-clinical     study items	• Sponsor Confirm request for study Sign contract for non- clinical study and initiate study

## **FDA Consultation Service**

Аррі	IND roval Plan	Early Stage Development Consultation
D	t&CRO	<ul> <li>Clarify project introduction</li> <li>Review drug / substance information and similar cases</li> <li>Provide authorized categorization and procedural information</li> <li>Propose non-clinical trial item(s)</li> <li>Consult primary study design</li> </ul>
	adyus esearch	<ul> <li>Gap analysis</li> <li>Review and develop consultation plan</li> <li>Identify category / track design</li> <li>Consult and confirm efficacy test design</li> </ul>



# Regulatory Affairs Center

#### Pharmaceuticals

Pharmaceuticals / Biologics / Cell therapy / Herbal medicines	
New drug/ IMD (Incrementally modified drug)/ Biosimilar/ Generic	Safety & Efficacy review/consulting (Non-clinical, clinical data)
	Specification & Test Method review/consulting
IND application	CMC/GMP Consulting
NDA / BLA application	• RMP writing
Common Technical Documentation (CTD) writing	DMF (Drug Master File) application

#### Medical Device/ Diagnostic Medical Device

1. Permission for Domestic Import/Manufactured Items
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- Item notification/certification/permission (medical device import and manufacturing)
- Medical device import/manufacturing license
- Quality system establishment consulting
- Diagnostic medical device

#### 3. Clinical trials

- Clinical development strategy
- management Advisory Establishment of clinical trial
- Plan Clinical trial plan, IRB approval
  - Writing report

2 0	VARCARE	certificati	ion corvi
2.0	verseus	certificati	John Sch Vi

- USA : PMN, 510(k) and QSR (21 CFR 820) • Europe : CE Marking and ISO 13485:2016
- Medical device certification/permission by other countries such as Canada

STED	<ul> <li>Usability Engineering</li> </ul>
<ul> <li>Risk Management</li> </ul>	<ul> <li>Clinical Evaluation</li> </ul>
<ul> <li>Software Validation</li> </ul>	<ul> <li>Product Compliance</li> </ul>

#### 5. Quality system support service

· Statistical analysis, data

Monitoring Result

• KGMP

• ISO 13485:2016

#### FDA QSR-CE Surveillance Audit

MDSAP

# Clinical Trial Operation Center

#### STEP 01 STEP 02 Design Management Presenting a new design that Management through can increase the probability of discussion with experienced success (equivalent) through experts scientific evidence

#### **Regulatory Affairs**

- Regulatory and Market Access Strategies
- Product Registrations
- Regulatory Dossier Writing (CTD Packaging and CTD Writing)
- Gap Analysis
- Orphan Drug Designation
- CE Registration(MDR, based on ISO14155)

#### Pharmacovigilance

- Medical Assessment of adverse event
- Causality Assessment
- DSMB, IDMC, SRC Preparation and Management
- PV Writing : DSUR, PBRER, PSUR, RMP Writing
- Safety Database Maintenance (ARGUS, cubeSafety)
- MFDS Report : ICSR, SUSAR
- PV SOP Development and Training

#### **Data Management**

#### Data Management

- Design / Development of CRFs
- · EDC Set-up (Medidata, CRScube,
- Medical Coding (Certified MedDRA Coder)
- SAE Reconciliation

SafeSoft)

 Data Matrix Dedicated DM · CDISC(Clinical Data Interchange Standards Consortium)-SDTM(Study Data Tabulation Model)

Data Quality Control

- External Data Handling



#### **STEP 03**

#### STEP 04

Result

#### **DM/STAT**

Data managemen using various statistical techniques

Draw a conclusion with secure and reliable data and results

#### **Medical Affairs**

- Synopsis, Protocol Writing
- CSR Writing
- Clinical development consulting
- Medical monitoring for clinical trial
- Medical Consulting

#### **Clinical Operations**

- Specialized focus on tasks by dividing Teams
- Site and Investigator Feasibility
- IRB Affairs
- Study and Site Monitoring (Start up / PSV, SIV, SMV, COV)
- Unblind Part Operation
- Risk Based Monitoring

#### **Biostatistics**

- Statistical Consulting and Design
- SAP, SAR (Statistical Analysis Plan, Result) writing
- Sample Size Calculation
- Randomization & IP Management
- Interim and Final Statistical Analysis
- Additional Statistical Analysis (TLG generation)
- CDISC-ADaM(Analysis Data Model)



# **Regulatory/Medical Affairs Services**



#### Regulatory Affairs (with Dt&CRO Team and Global CRO)

- IND, IMPD, AUS IRB & Global Clinical Trial Application
- NDA, BLA, ANDA, 505b(2), MAAs, Generics, DMFs
- IND, IMPD, AUS IRB & Global Clinical Trial Application
- Dossier Review for special drug : Orphan Drug, Biosimilar, Fast Track, Break-though, Application & Dossier Maintenance, Review for each CTD Section
- eCTD Registration
- SEND

#### Non-Clinical Management & Consulting (with Dt&CRO Team)

- Non-Clinical Strategy
- Study Lab Identification, Non-Clinical Study Set-up, Study Monitoring
- Review and Writing of Non-Clinical Reports (Module 4)
- Gap Analysis for Non-Clinical trial results (with Global company)
- Writing of Module 2.4, and Module 2.6
- IB Writing

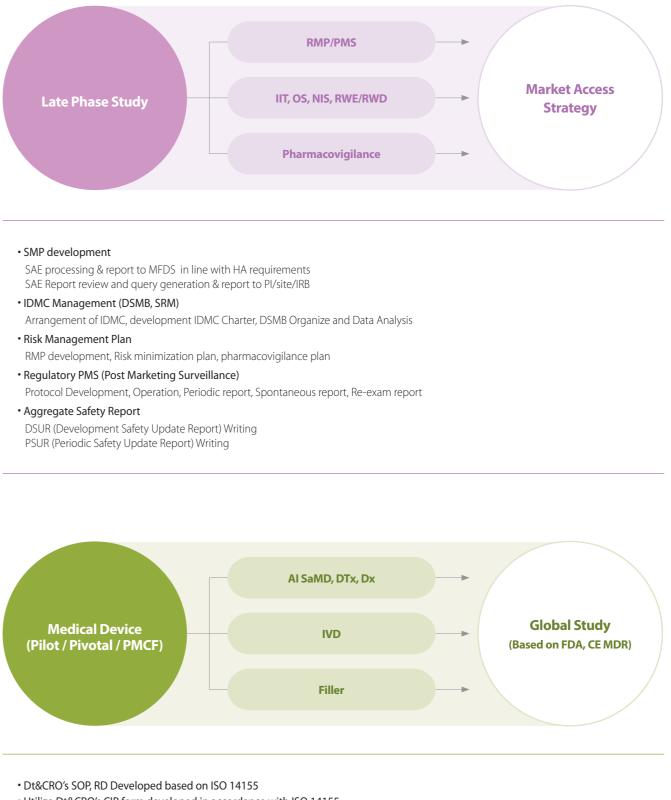
#### Drug Development & Strategy Consulting

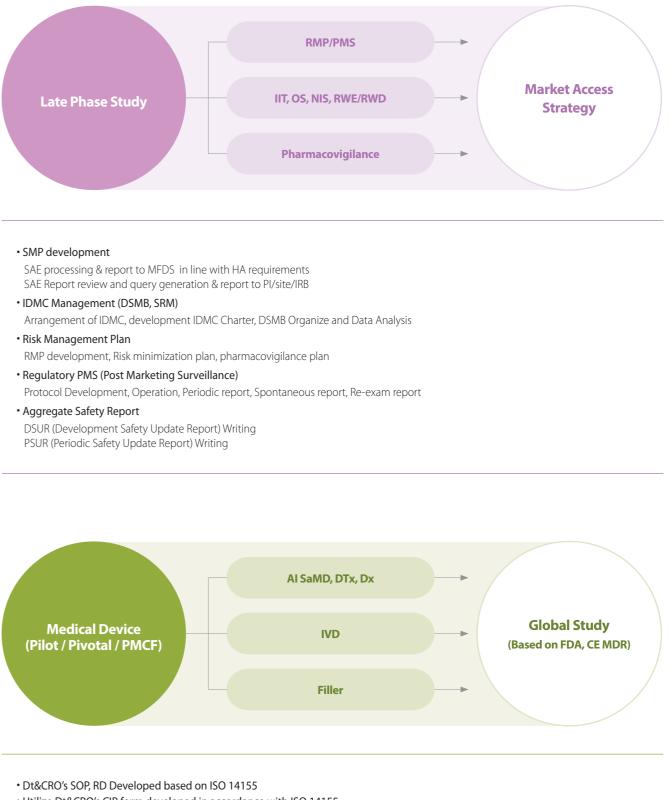
- Product Pipeline Development and Consulting
- Registration & Pipeline Development Strategy
- Regulatory Scientific Advice and Consulting
- · Agency Strategy and Interaction
- Pre IND Consulting
- FDA/EMA Advisory Committee Meeting Support

#### **Medical & Regulatory Writing Regulatory Publishing**

- e-CTD Submission
- CTD Packaging and Full writing
- CSR Writing for Publishing
- IB Writing

- DSUR/RMP/PSUR Writing
- Medical Monitoring Review Script
- Publication Manuscript
- Packaging Insert, Patient Information, Manuscript Writing





- Utilize Dt&CRO's CIP form developed in accordance with ISO 14155
- Annual Update of SOP, RD to meet NB's Latest requirements
- Close Relationship with Chung-Ang University and Korea University Through numerous Filler Experiences
- Dt&CRO's own Monitoring Room Reservation Process



LIMS

Improve reliability of tests by introducing Laboratory Information Management System (LIMS) automatically connected to Standard for Exchange of Nonclinical Data (SEND) when submitting US FDA.

System			
Animal room management program			
1 Clinical Pathology Program	4 Reproductive Toxicity Program	7 Genotoxicity Program	
2 Histotoxicity Program	5 Immunotoxicity Program	8 Safety Pharmacology Program	
3 General Toxicity Program	6 Local Toxicity Program	Environmental Toxicity Program	

**SEND Standard for Exchange** of Non-clinical Data

SEND is a digital file contains final report, SEND Datasets, Define file, nSDRG (nonclinical Study Data Reviewer's Guide), etc. which have major data such as general symptoms, weight, and pathology in non-clinical test data for FDA drug approval application. Dt&CRO provides high-quality services through the self-developed SEND software (Conversion Program), including non-clinical trial data conducted by other institutions as well as data conducted by other institutions.



## Real-time project schedule management program

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Management of Project Schedule

MoPS provides the progress of all projects to the client in real time. Customer communication program that allows you to disclose and check the progress of the project.

MoPS

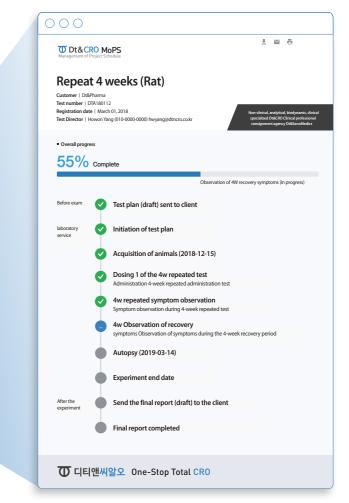
Links will be emailed to sponsors at the completion of key steps for each test item.

The desired test item can be displayed on the screen by clicking the ongoing project and can be printed or shared internally via email.

&CRO MOPS		🔹 🗃 One-Stop Total CRO		
nt of Project Schedule				
<mark>산절염치료제 안전성</mark> 바 (대명명역 변호) 다1940 (Ha (다1940 비호 (10-000-000) 변호 (10-000-000) 변호 (10-000-000)	시험			
일반독성 2 DTN180110 투여시험 (Rat)	일반독성           시참변호 DTN180111           단회투여시험 (Dog)	오만독성 시동번호 DTA180112 4주 반복 (Rat)		
🔏 🔮 최종보고서 완료 (완료)	100% 🛇 최종보고서 완료 (완료)	55% ···· 4₩ 회복 중심권할 (진행동)		
일반독성	수 유전독성	🔍 안전성약리		
<sup>호 DTN180113</sup> 반복 (Dog)	<sup>시험번호</sup> DTN180114 복귀돌연변이시험 (in vitro)	시험번호 DTN180115 Telemetry 시험 (Dog)		
) *** 4W 회복 중상관할 (완료)	100% 🔮 최종보고서 완료 (완료)	100% 🔮 최종보고서 완료 (완료)		

### Dt&CRO

#### Detailed progress status by test item



# 🛈 Dt&CRO

Location	Non-Clinical Trial Center		46 154-beon-gil, Yurim-ro, Cheoin-gu, Yongin-si, South Korea 17042
	Efficacy Evaluation Center	Ι	28 20-beon-gil, Baekryeong-ro, Cheoin-gu, Yongin-si, South Korea 17042
	Bio-analysis Center	I	28 20-beon-gil, Baekryeong-ro, Cheoin-gu, Yongin-si, South Korea 17042
	Clinical Trial Center	I	5F Youngchang Building, 10 Nonhyeon-ro, Gangnam, Seoul, South Korea 06247

**Contact**: +82 (0)31-322-2400

#### E-mail: info@dtncro.co.kr

### **Dt&C Group**

**Biotechnology Research Solutions** 

### **T**Dt&CRO

Non-clinical trials, Efficacy analysis, Bioequivalence, Clinical trials(Phase 1/2/3), LPS(PMS, OS, IIT etc) Full-service CRO

### **T**Huscience

Central Lab Method Development and Validation, Clinical Sample Analysis, Project/Sample and Data Management, Global Bio-Logistics **Tech & Electronics Development Solutions** 

### **T**Dt&C

Parent Company – KOSDAQ Listed Electrical testing and certification EMC, RF/SAR, Reliability, Failure analysis, IoT and Interface certification

### 

Rail, ICT Testing & Certification Domestic and international testing and certification services: EMC, RF/SAR, Safety



Software Authorization, Testing, Evaluation and Development **Dt&C** VINA Vietnamese Subsidiary

Testing, Certification and Inspection EMC of appliances. Safety and Inspection Services

### 

Japanese Subsidiary Software evaluation, Automotive testing, Software testing and verification, Electric EMC evaluation

### **Dt&C** CHINA

Chinese Subsidiary Testing and Certification

**Financial Services** 



#### Venture Capital Firm

VC Funding, Formation of Investment Associations, Local and Overseas Investment Consulting