



Welcome to NBF

A presentation by Dr.-Ing. Panit Kitsubun

BANGKHUNTIAN CAMPUS



Media Art & Media
Technology Programs:
MeA&MeT

School of
Architecture &
Design **SOA+D**

R&D & Pilot Plant: **EXC & PIP1,2**

Bioprocess Research & Innovation Building: **BRI**

School of Bioresources
& Technology: **SBT**

National Biopharmaceutical Facility: **NBF**

CES Solar Cells Testing Center: **CSSC**

OUR TEAM

✖ Multidisciplinary team: scientists, engineers

(KMUTT, BIOTEC, and others)

- Research and Technical staff 141:

✖ 60 Ph.D., 71 M.Sc., 10 B.Sc.

- Supporting staff 93:

✖ 7 M.Sc., 71 B.Sc., Others 15

BEC/BIOTEC: 20

Ph.D. 13, M.Sc.7

ECoWaste/BIOTEC: 7

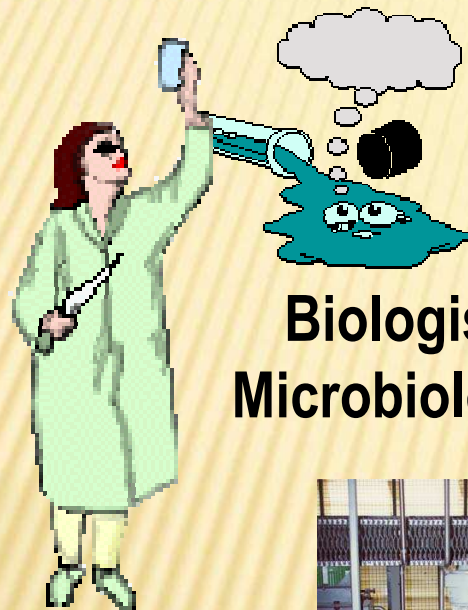
Ph.D. 6, M.Sc.1

✖ Attached students, science, engineering

- 277 (60 Ph.D. & 207 M.Sc.)

(Ph.D.: 25, MS: 71)

MULTIDISCIPLINARY CENTER



**Biologist,
Microbiologist**



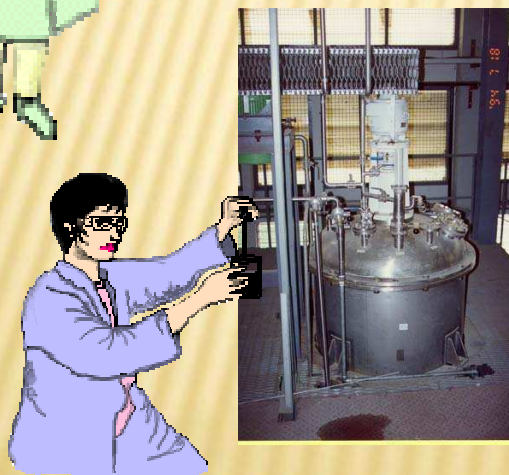
Bioinformaticians



**Chemist
Chemical structure**



Pharmacist



**Process engineer
Fermentation**

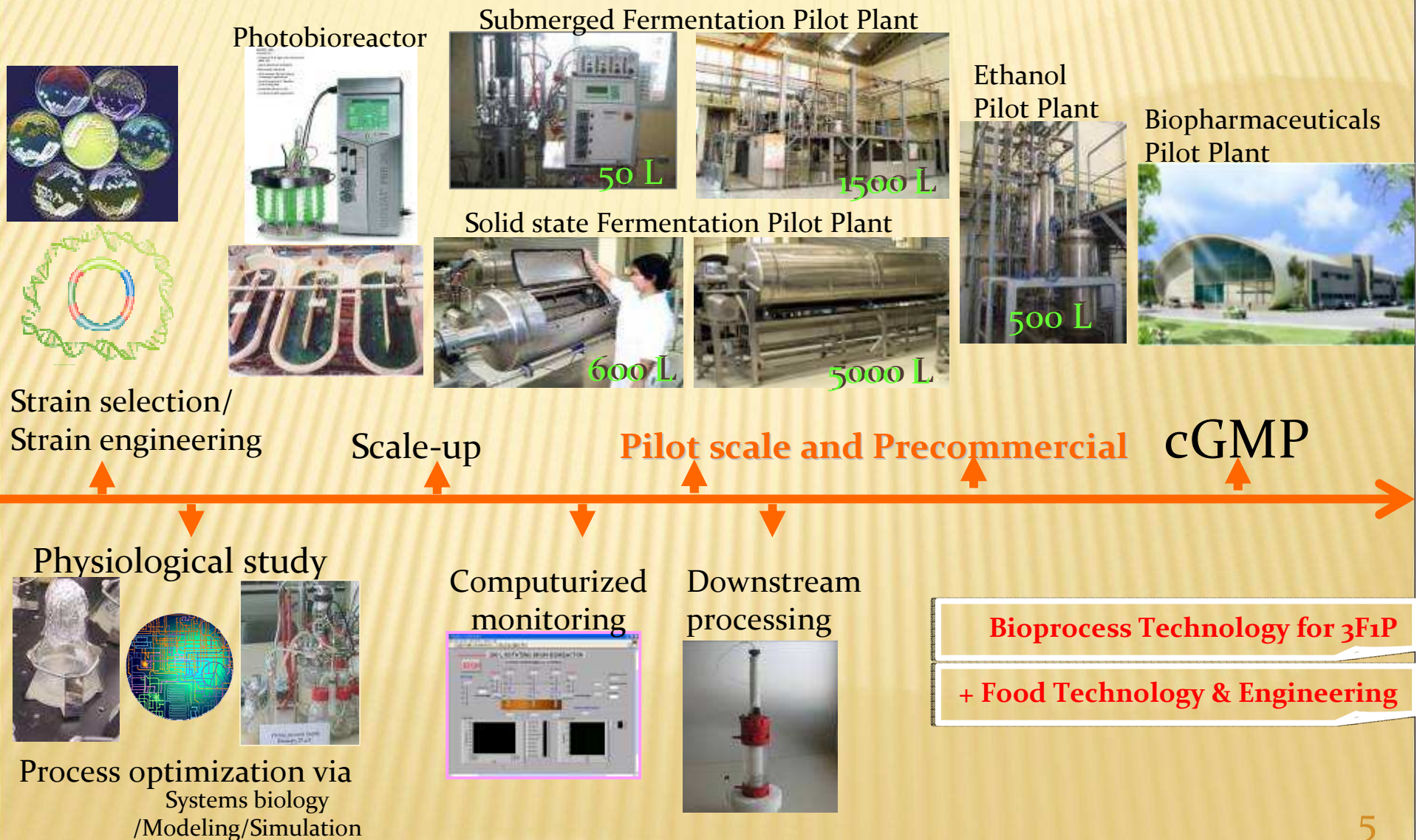


**Molecular biologist
Gene manipulation**



**Chemical engineer
Metabolic engineering**

TRANSLATIONAL VALUE CHAIN



BIOLOGICS: A \$145 BN GLOBAL MARKET



Class	#Launched	WW Sales US\$	No. Blockbusters	% Blockbuster Sales
rhProtein	65	\$52bn	13	80%
MAb	26	\$42bn	9	90%
Total	91	\$94bn	22	85%

- ✖ Approx. 15% of worldwide pharmaceutical market
- ✖ 15% annual growth (total market at 5%)

Source: IMS health, Newport Premium TM for Generics, TR research

RATIONALE OF THE PROJECT



Estimated value of drugs used in Thai hospitals in 2005 and 2006
(All imported)

ITEM	Value (Million USD)	
	2005	2006
EPOETIN ALFA	7.1	9.9
VACCINE, RABIES	5.6	6.9
INSULIN HUMAN ISOPHANE	6.7	7.2
MIXED INSULIN (HUMAN)	3.7	6.0
Total	23.1	30.0

Increase of approx. 30% over just one year!

MARKET SITUATION IN 2006

Top 10 products	Generic Name	Medical use /Treatment	Top 10 new products	Medical use /Treatment
1.Lipitor	Atrovastatin	Cholesterol lowering	1.Avastin	Colorectal cancer
2.Palvix	Clopidogel	Anti-platelet	2.Olmetec	Anti-platelet
3.Meronem	Meropenem	Anti-biotic	3.Amela-Ex	Anti-melasma
4.Celebrex	Celecoxib	NSAID	4.Tarceva	Cancer treatment
5.Eprex	Erythropoietin	Critical illness	5.Gammaraas	Immune globulin
6.Neurontin	Gabapentin	Epilepsy	6.Baraclude	Anti-viral/hepatitis B
7.Avandia	Rosiglitazone	Anti-diabetic	7.Prevnar	Heptavalent vaccine
8.Nexium	Esomeprazole	Dyspepsia, peptic ulcer disease	8.Prexige	NSAID
9.Tienam	Imipenem /cillastatin	Beta-lactum antibiotic	9.Velcade	Proteasome inhibitor
10.Crestor	rosuvastatin	Cholesterol lowering	10.Detrusitol SR	Anti-cholonolytics

PATIENT ACCESSIBILITY TO BIOLOGICS IN THAILAND



Drugs	Candidates for Usage (patients)	Current Usage (patients)	Patient Accessibility (%)
EPO	70,000	<26,000	<40%
GCSF	40,000	<3,000	<8%
Herceptin	12,000	<200	<2%
Rheumatoid related drugs	>200,000	<600	<0.3%

Source: Thailand National Cancer Institute and Thailand Rheumatic Society (2008)

THAILAND'S CURRENT ISSUES



- ✖ Biologics (except vaccines) are still 100% imported
 - + worth approx. \$1 bn in 2013.
- ✖ Health insurance issues:
 - + State employees enjoy full coverage
 - + Public sectors
- ✖ 30 Baht Scheme (Universal Coverage Program)
- ✖ Government encourages use of generics.
- ✖ Extensive R&D in tropical issues & generic drugs
- ✖ No capacity for translational research (production for clinical trials)

BIOLOGICS INCLUDED IN THE UNIVERSAL COVERAGE PROGRAM



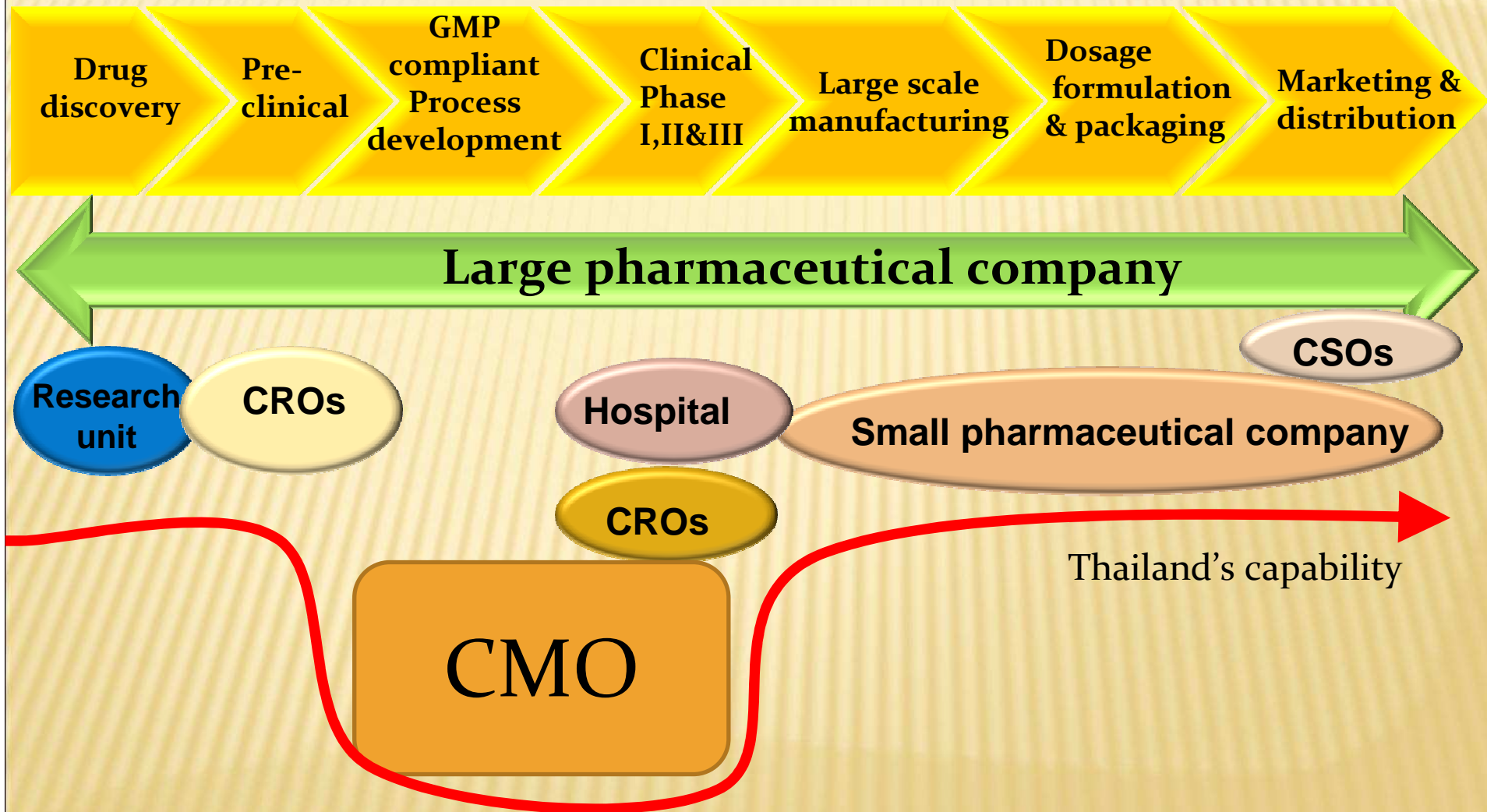
Drugs	Commercial names
Epoetin beta	RECORMON
Leuprorelin acetate	ENANTONE L.P.
Calcitonin salmon	MIACALCIC
Insulin	NOVORAPID PENFILL HUMALOG MIX 25
Hepatitis B Vaccine	HEPAVAX-GENE
Alteplase	ACTILYSE
Filgrastim	FILGEN
Lenograstim	GRANOCYTE INJECTION
Clostridium Botulinum Toxin Type A	DYSPORT

CURRENT BIOLOGICAL API PRODUCTION FACILITIES IN THAILAND



- ✕ Thai Red Cross
 - + BCG vaccine
 - + Plasma derived products
- ✕ GPO
 - + JE vaccine (mouse based)
- ✕ Greater Pharma
 - + House Dust Mite vaccine
- ✕ Department of Livestock Development
 - + Avian Influenza vaccine, HFMD vaccine, etc.

PHARMACEUTICAL VALUE CHAIN



CROs = Contract research organizations or Clinical research organizations
CMOs = Contract manufacturing organizations
CSOs = Contract service organizations

CMO IN SOUTHEAST ASIA

- ✖ A-BIO (Singapore, ceased operations)
- ✖ Inno Biologics (Malaysia, cell culture)
- ✖ Alpha Biologics (Malaysia, cell culture)
- ✖ LONZA (Singapore, large scale cell culture and microbial fermentation)

→ Only few CMOs offering manufacturing services for smaller batches

VISIONS



To boost Thailand's
translational and clinical
research activities



To form a linkage between the
R&D and commercialization



To enhance Thailand's overall
competitiveness in the
biopharmaceutical industry

MISSION



- ▶ To be Thailand's first research organization to produce clinical grade materials according to international standards (cGMP, USFDA, EMEA)
- ▶ To give services in process development ranging from laboratory to pilot scale.
- ▶ To give training and consultancy in specific technical and regulatory issues

NBF'S HISTORY



Funding from:

- Royal Thai Government
- KMUTT
- BIOTEC

Research funding from

- TCELS
- CPMO
- Private sector

2008

- Project initiation in 2008

2009

- Initial Funding

2010

- Construction of NBF building completed
- Microbial suite clean rooms completed

2011

- Start equipment acquisition

2012

- Soft opening in 2012

2013

- Construction of Cell culture suite clean rooms
- Equipment acquisition for cell culture suite

WHO ARE WE?

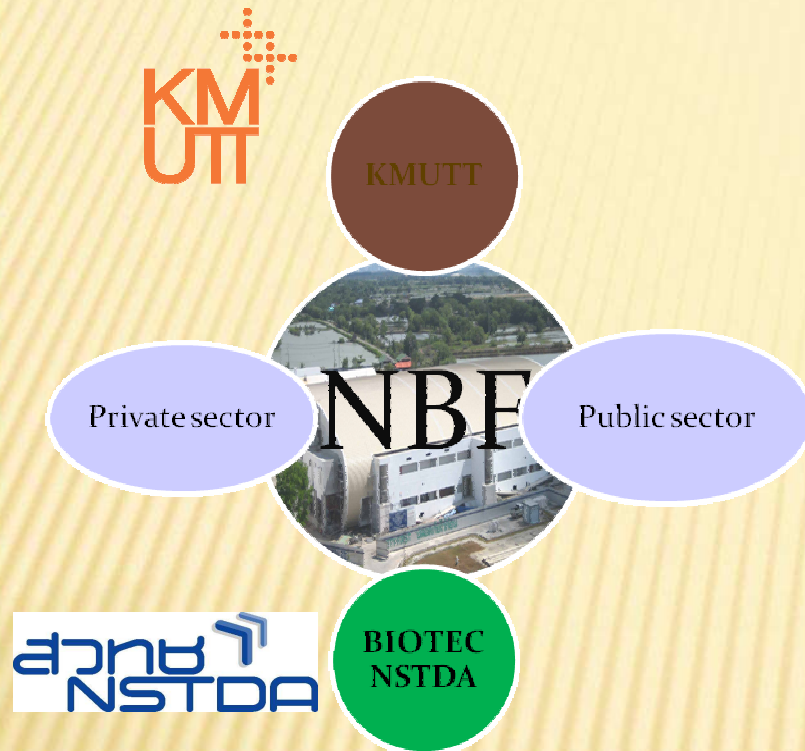
- ✖ Thailand's first CMO
- ✖ Thailand's first producer of recombinant drugs for clinical trials
- ✖ Contract Research And Manufacturing Services (CRAMS)
- ✖ >50 FTE scientists and engineers



KEY TO SUCCESS

- ✖ National facility & national agenda
- ✖ GMP standard (PIC/S, EMEA and USFDA)
- ✖ Qualified personnels
- ✖ Adequate and efficient public relations
- ✖ Financial self-sustainability in the long run
- ✖ Commitments from stake-holders (KMUTT, BIOTEC/NSTDA and MoPH)

MANAGEMENT OF NATIONAL BIOPHARMACEUTICAL FACILITY



- ▶ Self-sustained organization, where profit is not the primary goal
- ▶ Venture philanthropy concept
 - ▶ Investment by the government including some seed funding
 - ▶ Widely utilized in healthcare/medical research Translational research



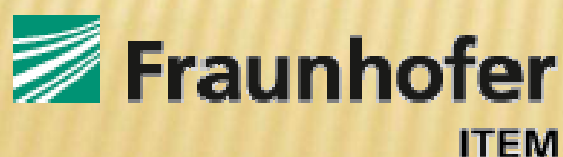
OUR ALLIANCE



Berli Jucker Public Company Limited
บริษัท เบอร์ลี่ ยุคเกอร์ จำกัด (มหาชน)

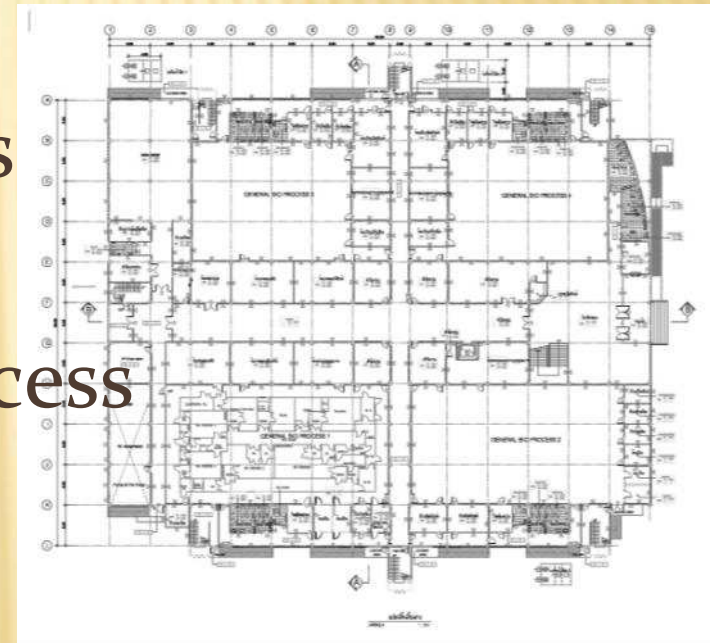


สถาบันวัคซีนแห่งชาติ
National Vaccine Institute



NBF: GMP FACILITIES

- Total utilizable area : 10,000 sqm
- Unit I-Microbial Bioprocess
 - Area: 600 sqm
- Unit II-Cell Culture Bioprocess
 - Area: 800 sqm
 - Automatic vial filling



UNIT 1: UPSTREAM PROCESSING

- Bioreactors
 - Up to 500 L working volume
 - CIP & SIP capable
 - Online monitoring of process parameters
- Centrifuges
 - Continuous (Alfalaval)
 - Floor-type



UNIT 1: DOWNSTREAM PROCESSING #1

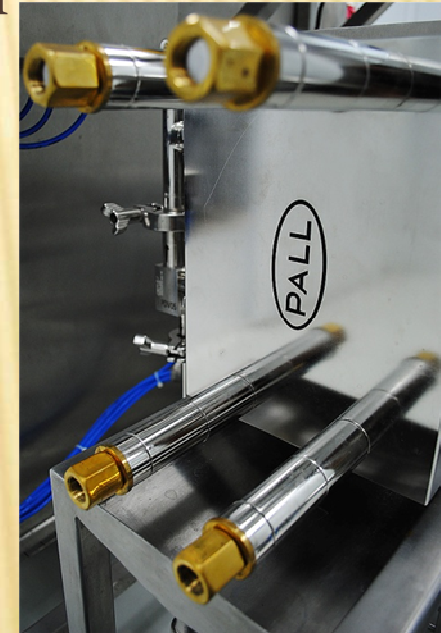
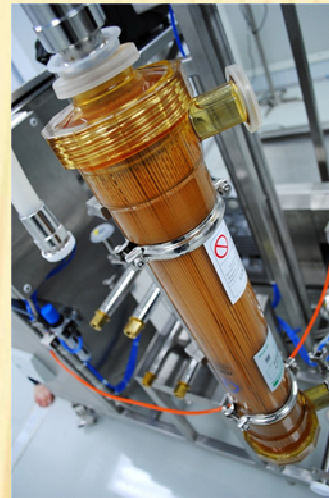
- ✕ Chromatography techniques
 - + Ion exchanger
 - + Affinity
 - + Hydrophobic interaction
 - + Gel filtration



UNIT 1: DOWNSTREAM PROCESSING #2

✖ Tangential Flow Filtration Concentration

- Diafiltration
- Clarification
- Depyrogenation
- Desalting



✖ Membrane

- Ultrafiltration, max. membrane area 5 sqm.
- Microfiltration, Hollow fiber

CELL CULTURE PRODUCTION UNIT 2

- ✖ Fully equipped cleanrooms grade B, C and D
- ✖ Cell culture unit capacity up to 600L
- ✖ Downstream unit with microfiltration, ultrafiltration and chromatography
- ✖ Fully automatic filling line for vials (6000 vials/h)
- ✖ Freeze drying capability



QUALITY ASSURANCE UNIT



✖ Documentation

- ▶ Quality Manual (QM)
- ▶ Site Master File (SMF)
- ▶ Validation Master Plan (VMP)
- ▶ Standard operating procedure (SOP)
- ▶ Batch release, record

✖ Raw material handling

✖ Environmental monitoring

QUALITY CONTROL LABORATORY

- Chemical QC Lab
 - ~ GC-TOF-MS
 - ~ HPLC
 - ~ LCMS
 - ~ TOC Analyzer
 - ~ Wet Chemical Analyzer
 - ~ Air borne particle counter
- Biology QC Lab
 - ~ Microbial Air Sampler
- Sterility Test
- Stability Test
- ELISA
- Animal testing to be outsourced



PROJECTED OUTCOME OF NBF

- Better accessibility to biologics by the Thai population
- Reduction of import of biologics worth at least 30 M USD per year
- Enhanced competitiveness of Thai pharma industry
- Pharma security (Public health security)
- Commercialization of at least 5 new products in the next 5 years
- Foreign investment in related fields worth not less than 100 M USD
- HRD development: 20 experts in related fields per year

TIMELINE

- ✖ Soft opening
 - + In 2012
- ✖ Official Opening
 - + March 24, 2014
- ✖ Manufacturing License (2014)
 - + Microbial production of API
 - + Cell Culture production of API
 - + Aseptic Filling
 - + Repackaging





THANK YOU!

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