

**Advanced health biotechnologies in Thailand:
State of the art, future trends and strategic preparation**

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I. Rationale

Rapid development in bio-engineering, molecular biology and genome sciences has been observed in the past decades. These advances have fostered innovative clinical interventions, including advanced therapies which target impaired or malfunctioning genes, cells and tissues of human body. Application of such treatments is expected to increase the possibilities not only to cure many common and rare diseases, but also to avoid serious adverse consequences of some medicines (Hernandez 2005; Wizemann and Berger 2010; Wobus and Boheler 2005). For example, stem cell techniques have been researched for treatment of degenerative disorders and traumatic organ damage.

Despite the notable benefits, international experiences suggest that potential implications and challenges, in several aspects, related to the technologies need to be considered. These issues include, for instance, allocation of scarce resources to research & development (R&D), ethical concerns for recruitment and protection of clinical trial subjects, manufacturing and quality assurance standards, intellectual property rights protection, misuse of personal genomic information, product approval, marketing regulations, value for money and budget impact, and accessibility to treatment among the needy population (Greenbaum 2008; Mintrom 2009; Tucker 2008). This means that appropriate policies, including laws, strategies and guidelines, have to be carefully devised and enforced at different levels.

Although Thailand has been classified as technology-recipient country, biomedical research is well developed in many areas. Excellence centers for medicine and pharmaceutical research have been operating in universities and other institutes, some of which have R&D capacity for advanced health biotechnologies. Many pilot studies and clinical trials have been conducted in university and private hospitals on diseases such as ischemic heart disease, stroke, motor neuron disease, diabetic ulcers and osteoarthritis. Furthermore, a number of private companies for stem cell research are operating (Marshall Cavendish Business Information 2010). Pharmacogenomics, and personalized medicine in general, is another area of research, with support from Thai government agencies (Biotec 2007; Faculty of Medicine Ramathibodi Hospital). Besides research initiatives introduced in the Thai setting, the

multinational industry has been interested in importing commercial products in these categories into the country.

Like in other countries, expansion of advanced health biotechnologies in Thailand raises serious concerns about their potential undesirable impact and imbalance between technology development policies, health protection and ethics. The limited literature and various newspaper articles suggest that, although at least four authorities- namely the Thai Food and Drug Administration, the Department of Health Service Support, the Medical Council, and the Health Ministry's Ethics Committee for Research in Humans-, have introduced many regulations concerning stem cell research and services (Bundittanugula 2010), it seems that these existing policies are inadequate (BBC 2010; Sipp 2009; The Nation 2010). At the same time, there are concerns about the possibility that stringent control imposed by the national bodies will hamper legitimate research, scientific achievements and benefits to the health of Thai people. Given that Thailand is a lower middle-income country, the investment in R&D and service provision of these expensive treatments requires evidence to inform policy decisions. Moreover, in a context where equitable access to healthcare has been ensured as a basic human right according to the Constitution, whether the three major public health insurance plans could afford and should include these technologies in their benefit package is another issue in question.

Aiming at appropriate preparation for the future development of individualized and regenerative medicine (in particular, gene, stem cell and tissue engineering therapies), this study will provide an insight on respective elements necessary for national policymaking in Thailand. It will recommend appropriate policy goals and instruments to be adopted in five inter-related areas, namely R&D, regulations, economics, education/information, and implementation.

II. Aims and objectives:

The aim of this project is to analyze the current situation of advanced health biotechnologies in Thailand and anticipate developments in this area in order to devise appropriate policies.

Objectives:

1. To review the present situation of advanced health biotechnologies in the world leading regions (i.e. the United States of America, and the European Union/European Economic Area) with regard to:
 - i) state of the art of technologies
 - ii) use/treatment benefits
 - iii) Related public policies: classified according to a framework adapted from Haga and Willard (2006) into R&D, legal/regulation, economics, education/information, and acceptance/implementation (including controversies)

- iv) If relevant information is available, the current R&D capacity in neighboring countries (e.g., China, Singapore, Malaysia, Vietnam) will also be reviewed
 - v) Working definitions of advanced health biotechnologies (regenerative and individualized medicine interventions)
2. To review the foresight studies produced on advanced health biotechnologies in these regions, focusing especially on abovementioned issues-- i), ii), and iii);
 3. To analyze past/current experiences of advanced health biotechnology and policy development in Thailand, by using 2 case studies: genetic screening for thalassemia, and pharmacogenomic testing for susceptibility to Stevens-Johnson syndrome with the use of carbamazepine and phenytoin. Although the former biotechnology to identify a single-gene disorder has been available since the 1970s and may not be considered advanced, it is an essential component of an emerging field of personalized medicine at public health level (Public Health Genomics) and therefore appropriate for inclusion.
 4. To analyze the current situation of advanced health biotechnologies in Thailand in a parallel manner as done in selected countries/regions;
 5. To formulate policy recommendations in the areas mentioned in iii), based on the above findings and with a special emphasis on implementation planning.

III. Working definitions

A priori, *advanced health biotechnologies* will include:

a) *Regenerative medicine*: in particular, advanced therapy medicinal products as classified by the European Commission. Conventional regenerative therapies, such as growth factors will be excluded.

- Gene therapy: gene therapy products are biological medicinal products and hence need to be of biological origin. Gene sequences, which have been produced synthetically, such as synthetic oligonucleotides, are excluded from the definition. Gene therapy products consist of recombinant nucleic acids administered to humans with a view to regulating, repairing, replacing, adding or deleting a genetic sequence, and whereby its effect relates directly to the recombinant sequence or the product of genetic expression of this sequence. Novel recombinant or vector-based vaccines against infectious diseases are also specifically excluded from the definition of gene therapy products.
- Stem cell therapy: (Somatic) cell therapy medicinal products contain or consist of substantially manipulated cells and have properties for treating, preventing, or diagnosing a disease through the pharmacological, immunological and metabolic action of the cells or tissues. According to the definition cell therapy medicinal products need to be substantially manipulated in order to distinguish them from transplantation products (Jekerle et al 2010).
- Tissue engineering therapy : a product that “contains or consists of engineered cells or tissues, and is presented as having properties for, or is used in or administered to

human beings with a view to regenerating, repairing or replacing a human tissue. A tissue engineered product may contain cells or tissues of human or animal origin, or both. The cells or tissues may be viable or non-viable. It may also contain additional substances, such as cellular products, bio-molecules, biomaterials, chemical substances, scaffolds or matrices” (European Commission, 2007)

b) *Personalized medicine*, as defined comprehensively by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) as the “use of genetic or other molecular biomarker information (e.g., genomic, proteomic, metabolomic) to improve the safety, effectiveness and health outcomes of patients via more efficiently targeted risk stratification, prevention and tailored treatment management approaches” (Faulkner, 2010)

This definition includes both interventions at public health (e.g., population risk stratification, genetic screening) and clinical level (e.g., genetic profiling, co-dependent therapies consisting of a pharmacogenomic test plus a medicinal product).

[Please note that there may be overlap between this concept and the previous therapies and among the previous therapies themselves].

Definitions of these biotechnologies will be reviewed, including their weaknesses and strengths, in order to propose and validate among stakeholders the most appropriate terminology for the Thai setting.

IV. Methods

1. Document review: relevant policy-related literature concerning issues addressed in objectives 1, 2 and 3 will be extensively searched through both electronic databases such as Medline, Scopus and ClinicalTrials.gov as well as general search engines, namely Google, using appropriate key words. In addition, researchers will manually search for relevant reports/policy documents published by relevant authorities, e.g. the World Health Organization (WHO), International Conference of Harmonization (ICH), the US Food and Drug Administration (Cellular, Tissue and Gene Therapies Advisory Committee), the National Human Genome Research Institute of the National Institutes of Health (U.S. Department of Health and Human Services), the US Institutional Review Board, the Office of Science and Technology Policy, the European Medicines Agency (EMA) (Committee on Advanced Therapies), the European Commission/European Parliament, the Council of Europe, the European Public Health Genomics Network, the Institute for Prospective Technological Studies, the State Food and Drug Administration of the P.R. China, the Thai National Center for Genetic Engineering and Biotechnology (BIOTEC), the National Science & Technology Development Agency (NSTDA) and other academic institutes. Specific information on advanced health biotechnologies, such as overview of R&D, use, policies, responsible authorities, current performance of the policies, advantages/disadvantages of these policies, will be extracted using the dummy tables 1-3 (see below in the expected output section). Experts from neighboring countries (Malaysia, Singapore, Vietnam, China) will be contacted for information on current R&D capacity.

However, document review will be limited to literature published only in English, Spanish, Dutch, and Thai.

2. In-depth interviews: relevant medical experts, other stakeholders (e.g., social activists, representatives from private sector, and policy makers) and key informants from the National Science Technology and Innovation Policy Office (STI) will be interviewed to gather information and views on the current situation/activities and future direction of advanced health biotechnologies in their own institutes (if relevant) and the country.
3. Case study approach: to explore the barriers and facilitators of adoption/diffusion of advanced health biotechnologies in Thailand.
4. Stakeholders meeting: consultative stakeholders meeting(s) will be convened:
 - To gather information on the current Thai situation by experts (basic, translational and clinical researchers, other stakeholders, such as decision makers?)
 - To prioritize and narrow down the scope of the project if necessary and whether the priority setting approach should be technology-driven or disease-driven. Also the terminology framework for advanced health biotechnologies will be validated.
 - To present preliminary results of this study. This meeting is to verify/validate results, explore research gap, and fine-tune study recommendations.
 - Likewise, the final policy recommendations arising from the study will be subject to a consultation among stakeholders.

The following stakeholders groups are potential candidates to participate in the consultations:

1. Policymakers, especially from the health (MoPH, NHSO, Bureau of the Budget, National Neonatal Screening Programme), science and technology (STI, National Research Council), financial (MoF) and education sectors (MoE, Universities Council)
2. Regulators/legislators, such as the Thai FDA, Medical Council regulatory committee, national legislators, National Committee for Ethical Approval of Research in Humans
3. Health biotechnology academic institutions, including research groups working at hospital level
4. Health professionals, e.g., clinical geneticists, genetic counselors, clinical pharmacologists, clinical biochemists, hematologists, internists, cosmetic surgeons, clinical pharmacists
5. Industry representatives, including “big pharma”, biotech small and medium enterprises (SMEs), private hospitals and medical device manufacturers.
6. Health communication experts
7. Legal experts
8. Health economists
9. (Bio)ethicists/theologians/religious leaders
10. Patients'/consumers' representatives, social activists

V. Expected outputs

This study will identify key stakeholders and recommend appropriate actions to be taken in the future (10- or 20-year timeframe) by those stakeholders in order to achieve optimal benefits and minimize negative consequences of advanced health biotechnologies in Thailand. In addition, this study will propose systems and mechanisms or business model to those stakeholders working together in development, delivery and integration of advanced health biotechnologies into Thailand's health care system, including an implementation plan.

Apart from presenting results to relevant stakeholders the deliverable package includes a research report and journal article(s).

Dummy table 1: List of advanced health biotechnologies in different stage of development and utilization

Type of technology	List of interventions at clinical trial phases I-II	List of interventions at clinical trial phase III	List of interventions available on the market	List of interventions reimbursable by public insurance schemes
Gene therapy				
Cell therapy				
Tissue engineering therapy				
Personalized medicine				

Dummy table 2: Detailed information of advanced health biotechnologies reimbursable in selected countries/regions

Type of technology	Description of interventions reimbursable by public insurance schemes			
	Start date	Details of indications	Evidence support for reimbursement	Uptake of the technology
Gene therapy				
Cell therapy				
Tissue engineering therapy				
Personalized medicine				

Dummy table 3: Policy framework addressing concerns over advanced health biotechnologies in selected countries/regions

Type of technology	Research (e.g., prioritization, subsidization)	Regulatory issues (e.g., IP, pre-clinical and clinical submissions, manufacturers, GMP certification, labeling and leaflets)	Economics (e.g., supply/demand, market value and pricing, commercialization, reimbursement)	Education/information (e.g., health professionals and the public)	Acceptance/implementation (e.g., risk communication, informed choice consultation, public adoption, privacy and confidentiality, human rights protection)
Gene therapy					
Cell therapy					
Tissue engineering therapy					
Personalized medicine					

VI. Timeline

<u>Research progression</u>	May	Jun	Jul	Aug	Sept	Oct
Proposal development						
Literature review						
Development of conceptual framework						
Development of interview questions/other methods						
Conduct of interviews/others						
Data analysis and presentation of preliminary results						
Writing-up, final validation and dissemination of results						

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