The majority of pharmaceutical companies in Taiwan are devoted to generic drugs. However, due to the relatively small size of the internal market as well as the continuous changes in national health insurance policy, the profits from local product sales by local companies are gradually falling. To maintain the business and sustainable management, these local pharmaceutical companies have to face the challenges of upgrading and transformation in order to enhance their capacities for competing in the global market.

Therefore, the government has had a series of revolutionary policies underway since 1980s to improve the entire pharmaceutical environment for the establishment of pharmaceutical infrastructure. All of these efforts will hopefully lead to the setup of a better infrastructure foundation fitted with national conditions. For traditional generic companies, quality demand is the key issue and can be improved through several stages of Good Manufacturing Practice (GMP) implementation in hopes of reaching the first-rate international standards. For the stimulation of new R&D, the coordination and integration of various resources among the different governmental departments has been initiated, with additions to the build-up and enhancement of the organizational system, legislations, technology transfer mechanism, fundamental facilities, investment, manpower for biotech skills, international cooperation etc.

All of these endeavors are meant to make Taiwan’s pharmaceutical industry have a foothold in the global pharmaceutical mainstream, and also to hopefully commercialize R&D production in the newly emerging biopharmaceutical field in the near future. Under the encouragement of the government’s action plans on the management system, legislation, and incentive policy, described below are the R&D strategies and infrastructural construction reforms in recent years.

Improvement of Pharmaceutical Manufacturing Quality
There were three improvement stages in the quality management of drug manufacture. In the first stage, the Department of Health (DOH) announced the GMP guideline in 1982 and required sponsors to submit a Pharmaceutical Plant Master File (PMF) of foreign pharmaceutical factories for review in 1988 in order to provide a unified quality management for domestic and foreign drugs. To integrate resources as well as encourage domestic, GMP-unimplemented pharmaceutical factories to entrust drug manufacturing to GMP pharmaceutical factories,
the Drug Entrust Manufacturing Implementation Measure was promulgated in 1988. The stability testing guidance was announced in 1986.

The main goal of the second stage was management of the manufacturing process. The current Good Manufacturing Practice (cGMP) and the GMP validation guidances were announced in 1999. Domestic pharmaceutical factories would need to meet validation requirements in a three-stage timeframe by July 2004. Factory validation requirements for foreign pharmaceutical factories were announced in 2001, and comprehensively finished imported drug product validation would need to be met in a three-stage timeframe by the end of 2005. The stability testing guidance was amended and announced in 1998.

The goal of the third stage was to establish a management system in accordance with international levels. Except for comprehensive completion, the process validation of domestic and foreign pharmaceutical factories, the Pharmaceutical Factory Establishment Standards (including GMP and cGMP), and the revised drug stability testing guidance were announced in 2005. To ensure conformance with international norms, the DOH is actively pursuing accession for Taiwan to the Pharmaceutical Inspection Convention/Pharmaceutical Inspection Cooperation Scheme (PIC/S). Successful accession will help Taiwan reach the global standard of excellence in pharmaceutical inspection.

**Surveillance and Management of Drug Safety**

Since the announcement was made on July 7, 1993, clinical trials for new drug applications must be conducted domestically. License holders of new drugs are required to provide the latest domestic and foreign safety reports of their products every six months in a 7-year drug surveillance period. In 1998, the Chinese Clinical Association was entrusted to establish the National Reporting System of Adverse Drug Reactions (ADRs) in Taiwan (passive report). According to the Pharmaceutical Affairs Act (amended in 2004), guidance for the reporting of serious adverse drug reactions was announced, with mandatory reporting of serious adverse reactions of all approved medicinal products. By means of the ADRs reporting system and the Periodic Safety

Updated Report (PSUR) for medical products under the monitoring stage, the appropriateness and safety information of domestic new medicine uses were gradually established, as was the design of drug reassessment mechanisms.

**Upgrading of R&D Innovation in the Biotech and Pharma Industry**

The pharma industry has existed for decades. However, since the emergence of the biotech industry in the past 20 years, the pharma industry has been gradually incorporated with biotech in terms of technologies and product development. Biopharma has become a “hot” area for the prevention and treatment of various diseases, and therefore a future star which many governments in the world are pursuing and investing heavily in. To upgrade the traditional pharma industry and advance biotech development in Taiwan, the government has drawn up policies with the expectation that both industries will thrive by 2010.

To advance the development of the biotech industry, the Executive Yuan proclaimed an “Action Plan for the Biotechnology Industry” and set up the Executive Yuan Biotechnology Industry Guidance Task Force in 1995. In 2002, the Executive Yuan issued “Challenge 2008 — National Development Plan”, in which both biotech and pharma industries are included in the crucial development projects, with the deliberate statement that biotech is one “star” in the government’s “Two-Trillion, Two-Star” project.

To enhance biotech development and upgrade the pharma industry in Taiwan, the Ministry of Economic Affairs (MOEA) made strategic plans that include the establishment of short-, mid-, and long-term development programs; improvement in coordination and integration among governmental departments and also with the industries; reinforcement of intellectual property; increase in implementation efficacy of the Science & Technology Development Programs and National Research Programs; encouragement of clinicians’ involvement in clinical trials; increased transparency of the Pharmaceutical Benefit Scheme for National Health Insurance; interdisciplinary cooperation with other industries; impetus for international certification and harmonization; assistance in product commercialization; etc.
The MOEA's Pharmaceutical Industry Assistance and Promotion Project was set to aid technology development in industry, strategic alliance and international cooperation, and personnel training, with the goal of promoting technology and global competitiveness. In 2004, the MOEA and the DOH coordinated and set up a platform mechanism for communication between the industry and the governmental departments. The channel consists of three levels of communication meetings from the bottom-up direction, in hopes of providing solutions for the barriers facing the industry and understanding the needs and proposals suggested by the industry.

**Establishment of New Drug Discovery Capacity**

**Driving National Integrated Research Programs**

To build up Taiwan's biotechnology research capacity, the Taiwanese government integrated research resources from different departments in order to drive the huge, integrated, long-term biotechnology and national programs, which include the National Science and Technology Program for Biotechnology and Pharmaceuticals (NSTPBP) and the National Research Program for Genomic Medicine (NRPGM).

R&D for biotechnology and medicine in Taiwan is through a kind of sharing and collaboration system as shown in Fig. 1. The upstream, midstream, and downstream of the drug development value chain are supported by the National Science Council (NSC), the MOEA, and the DOH, respectively. In the upstream, basic research is conducted at Academia Sinica and universities. In the midstream, the projects related to technology application and development are executed by nonprofit organizations and state-operated business units. In the downstream, commercialization of the research result is driven by industry.

The NSTPBP is designated to advance R&D in Chinese herbal medicines, new chemical drugs, and also biotechnical drugs. The disease research fields include cancer, diabetes, and cardiovascular and neurological diseases. On the other hand, the NRPGM is focused on molecular mechanism research related to diseases and heredity in order to find the target (gene or protein) for curing the diseases or for acting as a diagnostic biomarker.

**Establishing the Infrastructure of Drug R&D**

Another important mission of the NSTPBP and the NRPGM is to establish the technology platform and core facilities for drug research and development. The core facilities of the NRPGM are to support the
related genomic research of universities, institutes, and industries. On the other hand, the NSTPBP has established core facilities such as a cGMP pilot plant for protein drugs, an AAALAC toxicology center, and a cGMP pilot plant for botanic drug products in order to provide an essential platform for drug development. To speed up drug R&D and link the industry value chain, the National Programs efficiently execute essential projects and utilize technology platforms through a virtual team collaboration model.

Establishing Clinical Trial Centers
To achieve the goal of setting up an international clinical trial center as well as to enhance the mechanism and monitor the control of national clinical trials, the virtual team for a new drug clinical trial center has already been deployed. First of all, the DOH amended and expanded the hospital level for executing clinical trials in 2005 in order to increase the execution rate and encourage clinical research at qualified teaching hospitals. In addition, the DOH supported medical centers to form a General Clinical Research Center (GCRC). Hence, four medical centers — National Taiwan University Hospital, Tri-service General Hospital, National Cheng Kung University Hospital, and Wan Fang Hospital — established Excellence for Clinical Trial and Research in 2006. The Center for Drug Evaluation (CDE) is entrusted by the DOH to understand the situation and demands of the medical clinical trial environment and clinical laboratory of the GCRC, consider international regulations, and address specific and feasible plans for guiding the auditing mechanism of clinical trial management quality.

Conclusion
According to the 2005 BTC conclusion, pharmaceuticals is designed to be a key industry by the Taiwan government. Therefore, the government is taking account of the pharmaceutical industry development. To promote the traditional industry upgrade and drive the upstream, midstream, and
downstream receiving and carrying mechanisms of new drug research results, the government has collected experts’ suggestions in the aspects of regulation, environment, capital, and business model for a gradual reform. Healthier and more fast-growing effects are expected in the pharmaceutical industry development. In addition, through advancing the export strategic alliance, the overseas market is expected to be expanded to carry export growth.

For the emerging biotechnology field, the government expects speedy commercialization through regulation and capital support. On the other hand, for the pharmaceutical field, the short-term goal is to develop niche items such as the patent-almost-expired active pharmaceutical ingredients (APIs), new formulations, new indications, and new combinations, etc.; the mid-term and long-term goal is to develop new drugs, including new chemical entities (NCEs) and biotech drugs. In the future, research collaboration and technology combination between these two industries will drive the long-term development of the national industry to promote Taiwan as the Asia Pacific planning and operating center for R&D, manufacture, and operation of the biotechnological pharmaceutical industry.

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