Korean J. of Toxicology
Vol.1, No.1, p 43-48, 1985

PROSPECT OF GOOD LABORATORY PRACTICE IN KOREA

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In the early 1970's, a new and somewhat unfamiliar word, GMP(Good Manufacturing Practice) was introduced into this country. Since then various investigations and studies as to the possibility of implementing this new idea have been made by academic circles, governmental regulatory agencies, pharmaceutical companies and other concerned groups. To the best of my knowledge, the Ministry of Public Health and Social Affairs began to formulate regulations around 1978, which recently resulted in legislation covering Korean GMP. In 1985 three facilities of the pharmaceutical industry were carefully evaluated and approved to be suitable according to the Korean GMP regulation.

During the past few decades, our pharmaceutical industries have developed tremendously in terms of pharmaceutical technology and increased production capacity. However our counterparts in other countries have presented marketing challenges to the export of our products throughout the world. It is true that under the policy of trade protection by our government, the pharmaceutical industry has grown without interferences and competition from abroad, but in the furture we must seriously consider the effects of new patent laws and free trade upon the industry. If our government agrees to adopt the patent law of new substances, it can be anticipated that the domestic structure of our pharmaceutical industry will be changed drastically. Therefore, it is obvious to us that our pharmaceutical industry and government policy makers should be ready to meet such challenges and pressures from the outside. In this regard, it seems to me that research and development in the pharmaceutical industry must be encouraged, promoted and supported by all the means at our command. By doing this, we can produce our own pharmaceutical products for sale in both domestic and overseas markets. As you know, developing a new drug is time consuming and requires highly educated research manpower as well as large capital investment. It is also necessary that new drugs be tested for effectness and safety by the industry.

To further emphasize the need for drug safety, I need only point out the tragic adverse effects caused by the use of Thalidomide by pregnant women in Europe and the United States in 1962, which resulted in the malformation of fetus. This occurred despite the fact that many toxicological studies, based on existing regulations, were carried out before the drug was approved for marketing. The regulations in force at the time did not prevent the resultant shock and tragedy. Because of the tragedy many countries reconsidered the safety guideline and started to formulate stricter regulations and scientific toxicological methodology in order to get safer drugs. In the late 1970's the U.S.A. published and enforced new guidelines for the toxicological evaluation of drugs. Soon after the Japan and many

advanced European countries adopted similar guidelines. In many advanced countries, the new safety guidelines, so called GLP(Good Laboratory Practice), have been expanded and applied not only to drugs, but also to foods, food additives, animal feed, and even house appliances. The basic idea behind these toxicological regulations is to avoid the potential adverse effects of chemicals before they are used in the clinic. These tests are essentially non-clinical laboratory experiments using experimental animals. The use of such screening techniques enable us to eliminate those chemicals that are potentially toxic. However, in order to maintain the quality and integrity of such nonclinical studies, the individual toxicologist and investigator should perform their work according to GLP regulations. In this manner their results can be reproduced by other laboratories.

Some brief examples of the scope of GLP and some toxicological tests required by the FDA in the U.S.A. and the Japanese regulatory agencies are shown in Tables 1 and 2. Table 3 shows the relationship between Phase 1 study and preclinical study. All toxicological informations and results obtained from animal experiment(preclinical tests) become the basis for Phase 1 toxicological tests. Since residues from agricultural pesticides, insecticides and other pollutant chemicals are recirculated through the biosphere resulting in exposure to human subjects, the current trend is to evaluate the potential hazards of these residues and environmental pollutants following the guidelines established by GLP. Tables 4 and 5 show the interrelationship between these chemicals and environment.

Table 1. Scope of Good Laboratory Practice

Food and Drug Administration	Japan
Food and Food Additive	Drugs
Coloring Agents	Chemicals
Human and Animal Drugs	Biological Substances
Medical Devices	
Biological Substances	
Electronic Appliances	

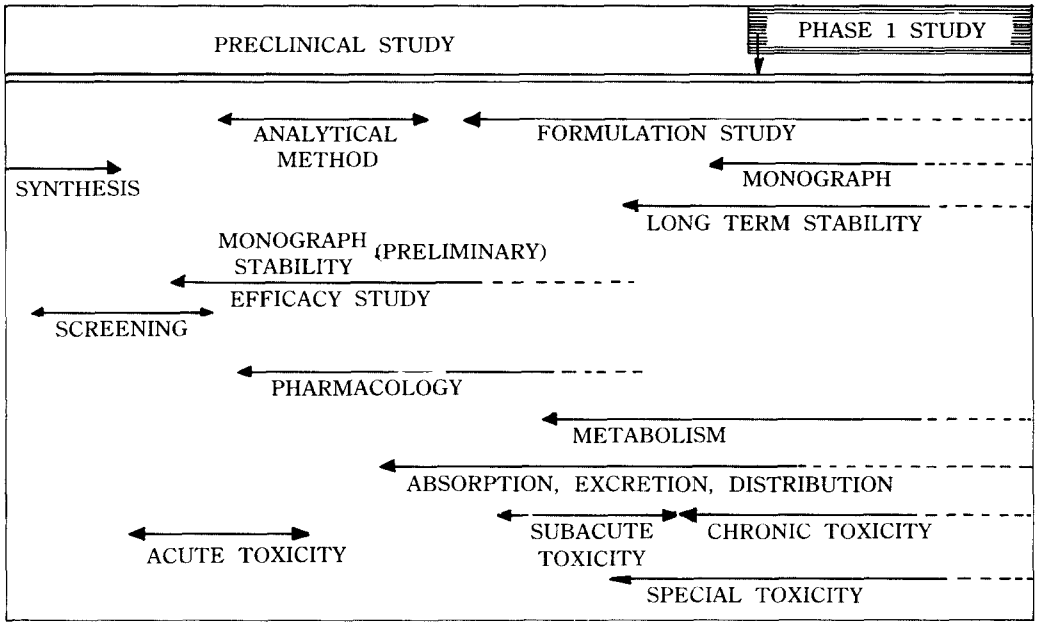
Table 2. Toxicological Tests

Acute Toxicity
Subacute Toxicity
Reproduction Toxicology-Fertility and General Reproductive Performance, Teratological, Perinatal and Postnatal Studies.
Carcinogenecity and Mutagenecity Studies
Dermal Toxiciity
Dependency Studies
Neurotoxicity
Inhalation Toxicity

I would like to describe our current regulations governing toxicological studies on drugs. In 1982 the NIH(National Institute of Health) established guidelines for general toxicological studies. This year it is expected that guidelines covering virtually all toxicity studies as shown in Table 3 will be promulgated. It is expected that these two guidelines will be eventually combined and legislation provided by

the Ministry of Public Health and Social Affairs as part of the Korean GLP regulations.

Table 3. Relationship Between Phase I Study and Preclinical Study



I believe it important to mention that the most emphasized thing about making new GLP regulations is that they must reflect our high industrial technology. We must determine whether or not we have qualified laboratories which can carry out toxicological investigations according to these perfect GLP guidelines. In addition, in the light of our present industrial status at such time as the GLP regulations are enforced, we must select which drugs and foods are subject to the regulations. In the case of new drugs, I would like to propose the adoption of the IND(Investigational New Drugs) system used in the U.S.A. which pharmaceutical firms and the FDA have designed for toxicological testings for certain drugs prior to market approval. If we do this, the pharmaceutical industry will save time and money.
The GLP regulation is concerned with many industrial products other than pharmaceuticals and foods as shown in Table 4 and 5. As a consequence there will be many different laboratories conducting toxicological studies, and therefore it is important that these laboratories be suitable for toxicity studies on drugs, foods and other commercial products in their concerns(Table 6). Usually the GLP regulation in each country specifies various requirements for the practice of toxicity studies, as shown in Table 7, in order that the data from their toxicological studies will be repeatable and reliable for other investigators. Consequently our GLP regulation should be recognized and accepted internationally. In this way any pharmaceutical products or foods approved as safe in Korea will be recognized as safe by the rest of the world and can be exported to international trade markets.

In this connection, I would like to discuss our present situation. As I mentioned

Table 4. GLP & Related Scope

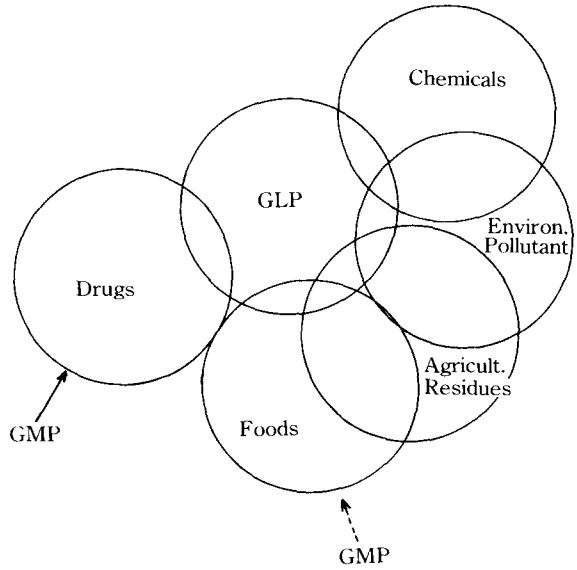


Table 5. Transport and Alterration of Chemicals in the Environment

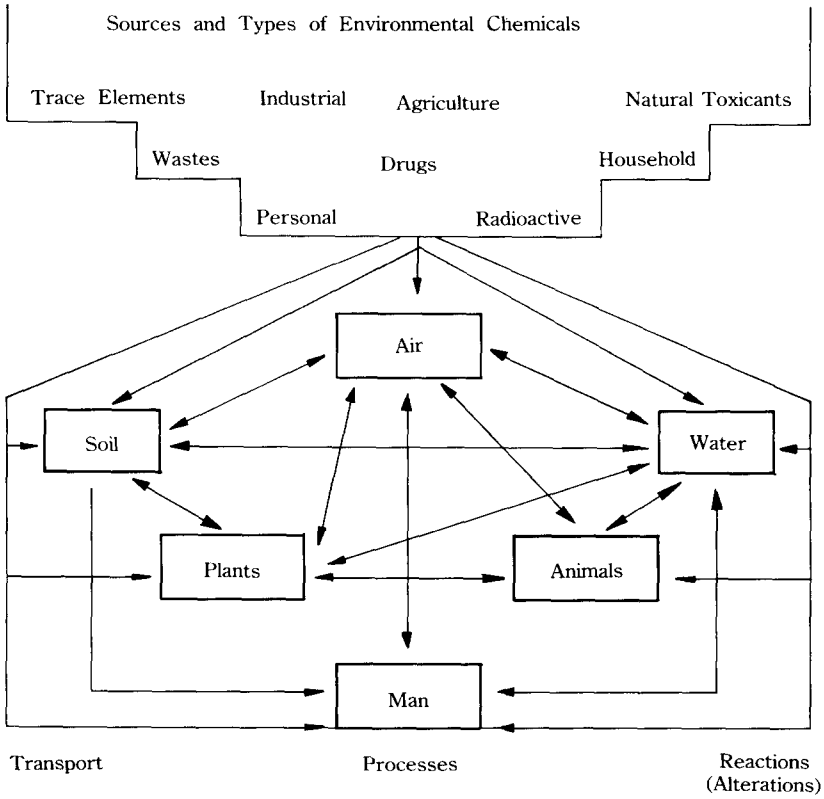


Table 6. Toxicology Laboratories for GLP Requirement.

Safety Research Center in NIH
Local Laboratories in Public Health Services
Laboratories of Private Toxicology Companies (Contract Base)
Laboratories in Universities
Laboratories of Pharmaceutical Industries
Laboratories in Ministry of Agriculture and Fisheries
Laboratories of Environmental Protection Agency
Laboratories in Ministry of Commerce and Industry
Laboratories in Ministry of Science and Technology

Table 7. GLP Contents*

Organization and Personnel
Facilities
Equipment
Testing Facilities Operation
Protocol for Conduct of Nonclinical Laboratory Study
Record and Report
Inspection

*The GLP contents should be acceptable internationally.

Table 8. Organization of Safety Research Centre

One Director in Department of Safety Research.
Five Division*; Safety Evaluation and Assessment, Toxicology, Pharmacology, Experimental Animals and Histopathology.
Computer Data Base Room.**

* Each division comprise a chief investigator and researchers. SPE laboratory animals are produced by the Division of Experimental Animals. Total research manpowers are twenties in this year.
**Toxiline will be connected from 1986.

previously, the Ministry of Public Health and Social Affairs has already started to formulate Korean GLP regulation. However, it is expected to take several years to complete. In the mean time the Safety Research Centre has been established under the auspices of the Korean NIH. Its organization is shown in Table 6. A new laboratory building comprising approximately 7,000 square meters, is now under construction (Table 9). It will have a clean room system(Class 1000) where SPF(Specific Pathogen Free) level laboratory animals will be bred and maintained. Ultra modern equipment and instruments will be available for use by the investigators. We expect that the building and facilities will be partially available by the end of this year.

As you well know, toxicological studies according to GLP regulation begin with laboratory animals. So it is obvious that we need a good quality of animals, the most desirable being SPF level ones. Unfortunately it is currently very difficult to obtain such experimental animals from domestic market. Therefore, the Ministry of Public Health and Social Affairs is presently preparing a regulation covering laboratory animals used by toxicologists. In this regard, I personally invite any suggestions or advice from the newly organized academic society, the Korean

Table 9. Facilities of Safety Center

	Clean Room (class 10000)	Non-clean Room
1st Floor	— Quarantine Room — Feed Preparation Room — Sterilization Room — SPE Animal Breeding Room	— Div. of Experimental Animal
2nd Floor	— Animal Breeding Room	— Library — Conference Room — Div. of Safety Evaluation — Direction's Office Room
3rd Floor	— Experimental Animal Room	— Inhalation Toxicity Room — Metabolism Study Room — Contaminated Toxicity Room — Autopsy Room — Div. Toxicology — Div. Pharmacology — Computer Room
4th Floor		— Genetic Toxicity Room — Electronic Microscope — Div. Histopathology — Central Instrumental Room — Monkey & Dog Room

Associations for Laboratory Animal Sciences.

In conclusion, I would like to summarize as follows:

1) The Korean GLP regulations should be recognized and accepted internationally.
2) This year the NIH will formulate tentative regulations which will then be turned to a review committee for study and discussion, allowing experts and specialists to make suggestions and provide constructive advice.
3) Even after legislation of the Korean GLP regulation, law enforcement will not be immediate, since our economic situation, the technical status in industry and other conditions such as manpower training must be considered first.

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