PHARMACEUTICAL

2014 was a year of transition, as the government made some significant adjustments in an effort to catch up with international regulatory standards.

The Committee would like to recognize the progress made by the Taiwan Food and Drug Administration (TFDA) in preparing for legal changes necessary to implement Patent Linkage (PL) and Data Exclusivity. Those initiatives will not only help Taiwan meet the requirements for entering into bilateral Free Trade Agreements (FTA) and multinational pacts such as TPP and RCEP, but will also enable Taiwan to create an environment that inspires and rewards investment in innovation. Fostering such an environment is especially important because new entities are being developed by local Taiwan biological companies for the international market. We expect the government to continue cross-agency collaboration to ensure that preparation of the PL mechanism moves forward expeditiously.

The National Health Insurance Administration (NHIA) also deserves commendation for such policy revisions as adoption of the use of drug comparators for the evaluation of new-drug pricing, and adjustment of the composition of PBRS (Pharmaceutical Benefit Reimbursement Scheme) committee membership to balance potential conflict of interest. Together, these changes have encouraged members of the R&D based

industry to continue their investment in Taiwan.

Nevertheless, R&D-based companies still have some major concerns related to new-drug reimbursement review practices. A substantial gap remains between the pricing level in Taiwan and that of the A10 countries which serves as an international price reference. Further, the timeline of the reimbursement review is unpredictable. These ongoing challenges have increasingly hindered companies in seeking corporate support to introduce new drugs to Taiwan. A concrete reimbursement timeline plan (such as the 60-90 days in Japan), along with a transparent tracking system and a value-based assessment mechanism for recognizing breakthrough innovation, would help greatly in resolving these issues. This solution could accelerate the introduction of new drugs in Taiwan to help patients with unmet medical needs.

Additionally, under the second-generation National Health Insurance reform, which tied the price adjustment mechanism to patent status, NHIA unfortunately only recognized compound patents registered in Taiwan, even though the Taiwan Intellectual Property Office (TIPO) recognizes many forms of pharmaceutical patents. After the pilot-run of the Drug Expenditure Target (DET), some newly approved items (or single-source drugs without substitution in the market) lacking a Taiwan compound patent were automatically defined in Category-3A and subject to immediate price cuts. Industry submitted proposals through various channels on how to recognize and reward innovation, but so far no government action has been taken. We urge the government to engage in dialogue with industry to generate a solution that respects IPR and ensures continuous availability of innovative drugs.

Even though both the TFDA and NHIA express a desire to accelerate the introduction of new drugs to Taiwan, there continues to be a one- to three-year delay in broad patient access after reimbursement because of the hospital listing procedure. The practice of limiting the number of items in the hospital formulary and of making profit-driven decisions on drug procurement, continues to be a big obstacle for patients, preventing them from utilizing the benefits the government wishes to offer. Considering the importance of this issue, we strongly recommend that the government keep moving forward with the implementation of Separation of Dispensing from Prescribing (SDP).

The R&D-based industry urges the Taiwan government to maintain an open dialogue with all stakeholders, and we will continue to do our part to support healthcare policy reform to enable the people of Taiwan to live healthier lives with the help of innovative and sustainable medicines. Our specific recommendations are listed below.

Suggestion 1: Build a transparent, predictable reimbursement review process to secure early access to innovative medicines.

The new reimbursement review system, which has now been in effect for two years since implementation of the second-generation NHI, has been marked by a low approval rate of new drugs and indications, unpredictable review delays, and the continuation of relatively low reimbursement prices without any sign of improvement.

Compared to the first-generation NHI, the review process for new drugs is now significantly longer. Reviews for new cancer drugs have been especially lengthy, averaging 726 days. The approval rate by the PBRS committee has been only 42%, and only 26% of the cases have been effectively reimbursed.

The situation has drawn attention to several key issues:

1. ***The two-tier system has become less transparent.*** The new system involves holding an Experts Meeting to provide preliminary opinions for new-drug reimbursement review and approval, followed by the PBRS committee meeting as the final decision-maker. The NHIA has suspended publishing minutes of the Experts Meeting, instead providing only the PBRS committee meeting record. But in fact the Experts Meeting focuses chiefly on professional and clinical aspects, while PBRS basically considers the budgetary and political implications. The public should be able to access the experts' perspective on the clinical value of new drugs, and to consider those professional opinions when examining the PBRS committee decisions.
2. ***Lack of clarity in reimbursement decisions has created unpredictable delays.*** In 2014, the PBRS committee forwarded a few new drug and indication cases to the National Health Insurance Committee (NHIC) for review due to budget concerns, which injected more uncertainty into the process. To control new drug expenditure, NHIA for years has been implementing a Price Volume Agreement (PVA) system, and PVA has become a recognized tool to mitigate the possible budgetary impact of new drugs. The PBRS committee action in forwarding cases to NHIC not only creates uncertainty and lengthens the process, but also reflects the lack of consistent principles underlying reimbursement decisions.
3. ***Absence of a mechanism to secure a reasonable timeline for new-drug reimbursement.*** From the patient's perspective, access to innovative medicine is a basic right. It may make all the difference in whether treatment achieves a positive outcome. However, no mechanism exists in the new system to monitor and examine the efficiency and performance of the new-drug review and approval process. We appreciate that the NHIA is planning to introduce an on-line system to track the progress of submitted cases, but at the same time it is crucial to establish a fast-track review for specific new drugs, as well as a risk-sharing

program or payer partnership program to accelerate new-drug review and reduce budget concerns. A reasonable new-drug review and approval timeline is essential.

4. ***Low prices for new drugs have impacted the sustainability of research-based pharmaceuticals.*** Currently, the average price of new drugs in Taiwan is only 51.8% that of the median for the benchmark A10 countries. As a result of this downward trend, the sustainability of the research-based pharmaceutical industry in Taiwan has been called into question. Price erosion has presented a harsh challenge for companies in the Taiwan market. All drugs have faced a price adjustment every year (through the current Drug Expenditure Target program) or every two years (as was done in the previous Price Volume Survey system). Highly restricted patented products are the only category receiving the price protection of the 15% "reasonable zone" (R-zone). Under these conditions, obtaining a high price when applying for new-drug reimbursement becomes critical for the viability of the entire product lifecycle. Over the past six years, however, only nine new drugs were granted "breakthrough" status, enabling them to be referenced with international prices. Other drugs were priced based on comparators, whose prices were quite low after going through many rounds of price cuts.

Recommendations:

1. ***Establish a reasonable timeline for review and approval of new drugs and indications.*** We suggest that the government cooperate with industry to set up a timeline for each step of the process, and provide a transparent monitoring system for all stakeholders. All decision-making during the process should be public and transparent, including the Health Technology Assessment (HTA) report, minutes of the Experts Meetings, and the PBRS meeting records.
2. ***Align with TFDA to adopt fast-track review.*** To accelerate patient access to innovative medicine, we suggest that NHIA adopt TFDA's fast-track review system for new drugs that treat severe disease, meet unmet medical needs, or have major clinical advantages.
3. ***Solicit patient opinions during new-drug review and approval.*** We suggest incorporating evidence from patients, including participation by patient representatives, in the new-drug reimbursement review process. A good reference would be the recent adoption in Scotland of a Patient and Clinical Engagement (PACE) system to provide for a comprehensive consideration of patient and clinical views.

Suggestion 2: Establish a fair, reasonable, and non-discriminatory price-adjustment mechanism for pharmaceutical products.

Since the 2013 *White Paper*, the Committee has been urging the government to develop a transparent, predictable, and reasonable model for price adjustments. However, the implementation guidelines currently in place under the DET price-adjustment pilot program have left uncertainty about the state of future patient care.

According to those guidelines, drugs in Category 3A – those that have been reimbursed within the past 15 years and whose compound patents have expired for five years – will only undergo a price cut within the 3% R-Zone. Although this situation is better than the 2014 DET cut, in which no R-Zone was provided, it does not really ameliorate the situation, since Category 3A suffered from the worst price reduction in the 2015 price adjustment: NT$8.21 billion, even after the 3% R-Zone was granted. The scale of cuts in 3A products exceeds 55%, which is far higher than for Category 1 or 3B. Moreover, for various reasons (such as having a New Chemical Entity patent in another country but not Taiwan), some additional new drugs fall into the 3A category upon reimbursement.

The low price level of 3A products has a major impact on overall new-drug pricing, since over 80% of that pricing is based on comparators drawn mainly from the 3A category. Granting only the 3% R-Zone to Category 3A products disproportionately impacts innovative, imported drugs and could wind up limiting patient access to innovative medicines.

Under the current system, the R&D-based pharmaceutical industry has been forced into a role of subsidizing the operation of hospitals, which demand discounts from drug manufacturers and then pocket the full reimbursement from the NHI (which later seeks to close the gap by cutting the reimbursement prices). These barriers, in addition to the relatively small size of the market and concern that low prices here will be benchmarked by other Asian countries, have given Taiwan a reputation as an unfavorable environment for investment in new-drug launches.

We urge the government to listen to industry concerns and fine-tune the DET guidelines. A win-win-win solution must be found that ensures top-quality medical care for the public, support for the government's efforts to control costs, and a sustainable business presence for the industry.

Recommendations:

1. ***Recognize all patents granted by the Taiwan government.*** Drugs that 1) have effective patents recognized by the Taiwan Intellectual Property Office (not just compound patents but patents of all kinds, such as those covering use or indication, formulation, process, or salts, crystalline, polymorph, etc.); 2) are receiving administrative protection against generic competition by virtue of having conducted

local clinical trials; or 3) still fall within the new-drug surveillance period should all be excluded from the periodic price adjustment and deemed as patented products.

2. ***Provide special consideration in price protection under DET to certain types of products.*** The Committee strongly recommends that all 3A products should be granted the 15% R-Zone. But at the very least, that treatment should be accorded to the following:
   1. **Items under data exclusivity or within the surveillance period.** The conditions of data exclusivity and surveillance period are granted by the TFDA. As the objective is to exclusively protect the data, there should be no generics on the market during this period. If these items exit the Taiwan market due to a significant price cut, patient access to medication will be impacted.
   2. **Items with Risk Management Plans.** Pharmaceutical companies make significant investments in implementing RMP for drug safety monitoring to reduce adverse effects on patents and help decrease NHI spending.
   3. **Items with process patents or product-by-process patents.** Process patents and product-by-process patents apply to biological products, as their patent protection is mainly based on the manufacturing process.
   4. **Items with formulation patents.** Formulation patents can enhance product stability, reduce the required dose, raise drug efficacy, and lower the incidence of adverse events.
   5. **Mono-source compounds.** Although the compound is off-patent, only a single source is available for the compound in the market in the absence of generics. If these items suffer significant cuts and exit Taiwan, patient access will be impacted.
   6. **Combos.** Though the items did not apply for ROC combination patents, one of the compounds is still patented and there is no generic in the market. It should also be deemed as "mono-source."
   7. **Items with new indication patents.** Such drugs target multiple treatments in different therapeutic areas.
   8. **Items with liposome composition patents.** ROC-patented items with liposome composition (with its compound) should be deemed compound patents.

Suggestion 3: Implement a rigorous system of Separation of Dispensing from Prescribing (SDP).

This issue has been raised in the Taiwan *White Paper* for many years. The existing system at Taiwan hospitals requires physicians to prescribe medicines listed in the hospital formularies, which are selected through a process based largely on the amount of profit to be gained by the hospital. Most hospitals also have a "one-in, one-out" policy to limit the number of items in the formulary, as well as a system of grouping medications with similar functions as a way to gain more profit. This approach may jeopardize patient access to the most appropriate medication for their particular conditions.

For the sake of patient-centric treatment, the government should build an environment in which hospital staff, doctors, and pharmacists are able to make professional judgments based on the welfare and individual needs of the patient. They should not be restricted to choose from among drugs procured for financial considerations, after the items have been accepted for reimbursement by NHIA. The problem is growing more serious. Besides the potential impact on the right of patients to access optimal treatment, it may also lead many international companies to decide not to list new drugs in Taiwan in the first wave, as the discounting requirement has made the net price in Taiwan the lowest internationally. The Committee appreciates the policy being followed by MOHW and NHIA in encouraging prescription releasing by public hospitals. However, the prescription-releasing ratio is still low after a several years of implementation. More importantly, one key element is missing from this policy: a prohibition on generic substitution. Without this regulation, community pharmacists may switch the drugs based on profit considerations, with serious risk to patients' health, rights, and benefits.

To correct the situation, MOHW and NHIA should consider different ways of compensating hospitals and general practitioners, so they do not have to rely on profits from drug dispensing. The role of dispensing should be primarily in the hands of community pharmacists, who can provide consultation to patients on medications and healthcare. A regulated margin for drug management should be made available to the pharmacies. The ban on generic substitutions should be clearly stated in the government's current communications to public hospitals and in future SDP regulations. SDP would empower physicians to prescribe the most appropriate medications based on their professional expertise. It also creates a mechanism to ensure that pharmacists review patient prescriptions to prevent any duplication or contra-indication between prescriptions from different physicians or hospitals.

Recommendations:

1. ***Eliminate the profit from drug dispensing.*** Set a clear principle to prevent hospitals from restricting patient access to reimbursed items based on profit considerations. Hospital fees should be adjusted to eliminate the reliance on profits from drug dispensing, and the release of hospital outpatient prescriptions to community pharmacies should become mandatory.
2. ***Establish concrete goals and timetables.*** Adopt an SDP roadmap so that the direction of implementation is clear,

even if it must be carried out in stages. An integrated implementation plan should include measurements of SDP compliance as part of the hospital accreditation system. It should be based on the number of prescriptions released and the number of pharmacists who are actually engaged in drug dispensing.

3. ***Engage in more public communication and education.*** Provide more extensive education to the general public about the benefits of implementing SDP. Patients should be helped to understand the crucial importance of SDP in improving the quality of medical care and decreasing the wastage of healthcare resources by reducing the volume of unnecessary medication. The result would be long-term savings for the NHI budget.
4. ***Set clear policies for implementation.*** Adopt clear regulations to ensure good dispensing practices by pharmacies and prevent drug substitution without doctor's consent, and set a policy of periodically publishing data on the amount of prescriptions released by individual hospitals.