

APPENDIX II

POST MARKETING SURVEILLANCE (PMS) GUIDELINES PHAP Circular No. 018-04

OBJECTIVES

These PMS Guidelines seek to enjoin all PHAP Member Companies to support and comply with the following objectives:

- To project the true scientific purpose of PMS studies. The PMS is primarily designed to allow physicians “to participate in appropriately designed surveillance studies (PMS studies)”, the purpose of which is to “to monitor the performance of the medicament under conditions of actual use.”
- To distinguish between true PMS and marketing-inspired activities being passed on as PMS. The latter come under various appellations such as patient clubs, seeding or experience trails, experience collection, product familiarization, et al.
- To rationalize current practices as to patient recruitment, remuneration, etc.

CURRENT SITUATION IN THE PHILIPPINES

- BFAD maintains a system of post-marketing surveillance and risk assessment programs to identify adverse events that did not appear during the drug approval process. BFAD uses this information to update drug labeling and/or to reevaluate the approval or marketing decision.
- Presently, BFAD allows new drugs to be registered under monitored release provided the registration holder submits a PMS sample size of 10% of estimated number of patients who will take the drug over a period of three years. Usually, 3,000 PMS case report forms over a period of three years (with an annual submission of 1,000 patient-CRFs) are required by BFAD. For orphan drugs or disease entities whose population size is small, the company may negotiate with BFAD to adjust the required number of patients in the PMS.
- Cumulative worldwide periodic safety update reports (PSURs) are also submitted to supplement the local PMS report.

- Pharmaceutical companies, in most cases, actively recruit patients (and physicians) in the PMS in order to expedite the data collection and meet BFAD's deadline. Physicians are enjoined to enroll their patients whereby product samples may be provided for patients' use, whether for full course of therapy or as starter dose. Physicians fill out a CRF that has been approved by BFAD for PMS purposes and these are routinely collected by the drug company.
- Patients under the PMS normally pay the physicians his usual consultation fee on a per-visit basis.
- Laboratory examinations may be conducted to complete the CRF depending on the requirement of the PMS protocol. Patients normally shoulder this expense as well.
- Pharmaceutical companies pay the physician a certain amount to compensate him for his participation in the PMS study. There is no standard amount paid to the physician and the fee may fall between 0 to 1,000 pesos per patient-CRF submitted by the physician. The company's medical director or suitable person designated to compile the PMS results conducts the quality check on the submitted CRFs for completeness of the data required. When the CRF passes scrutiny, then the physician is compensated for the CRF he has submitted.

POTENTIAL FOR ABUSE OR MISREPRESENTATION

BFAD rules and regulations stipulate only the MINIMUM number of CRFs that must be submitted by the company to fulfill the PMS requirement. Thus, a company may opt to continue the PMS beyond the required patient population for various reasons:

- Obtain more scientific data since the BFAD-required PMS population size may be limited statistically detect adverse events that will occur if more patients are included in the PMS.
- Continue the company-physician relationship under the aegis of the PMS whereby the company gains undue competitive advantage. It is at this point that allegations of influencing prescriptions may arise, which everyone knows and accepts, is against core principles of ethics of pharmaceutical marketing practices.
- Continue to compensate the physician per CRF submitted even past the BFAD-mandated minimum number of patients, resulting again in undue competitive advantage. At this point, we are treading dangerous ground in terms of bending ethics as it may alleged by interested parties that the company is now virtually or actually engaged in buying prescriptions.

SCOPE

- PHAP aims to remind its members that the basic principle of Post-Marketing Surveillance studies is that they must have scientific or medical merit, be objective, and not be designed for, or conducted as, a promotional exercise.
- The aim of PMS is to monitor efficacy and possible ADEs rather than to influence prescription habits of physicians.

SPECIFIC GUIDELINES

1. PMS are only allowed for products issued Monitored-Release (i.e., temporary) CPR. Products with Initial or Regular CPR (i.e., permanent) are not allowed to conduct PMS studies.
2. PMS studies must have a formal and valid research protocol that is approved by BFAD. This protocol should clearly state objectives, methods, planned analysis, sample size estimates, data collection forms and whenever necessary, consent forms for patients or their physicians. Consent for release of data should always be obtained from patients and a copy of such Consent Form should also be attached to the Protocol.
3. The protocol must include STUDY CLOSURE PROCEDURE which clearly states verbal or written explanations of alternative choices for treatment, including an option to discontinue the drug undergoing evaluation.
4. Whether patients are actively or passively recruited, the sponsoring company may supply drugs under PMS investigation, subject to the limits provided for by the Code governing samples (Section 9.0).
5. Whether patients are actively or passively recruited, the drug company MUST shoulder cost of diagnostic tests, visits and other intrusions that are required specifically for the purpose of the study, however, the patient should pay for other examinations routinely required.
6. PMS studies are for new products only; i.e, only those under monitored release. Conversely, products with regular Certificate of Product Registration (CPR) should not be put under PMS at all. The PHAP Ethics Committee may challenge a company whose PMS activity is doubtful and may compel that company to show the CPR of the questioned product.
7. Whatever the nomenclature, other post-marketing activities that do not fall under the PMS guidelines or which do not have a formal, proper and valid clinical study protocol (CT Phase 3b or 4), will be considered as marketing or promotional activities. As such, drug companies MUST NOT compensate physicians or patients who voluntarily join these activities. It is immaterial whether data collection is involved in these marketing activities and that the basic rule applies; no compensation is allowed.
8. Remuneration or compensation of physicians enrolled in a valid PMS should be reasonable. Moreover, such payments should not serve as an inducement to prescribe a particular drug. We submit the following guidelines:

- Pharma companies must exert its best effort NOT to compensate physicians who participate in the PMS, it being a scientific study that will benefit the physician's practice, the patients and the drug industry in general.
 - Where a compensation cannot be avoided, the amount must be kept to a reasonable amount depending on the amount of actual work that the physician is expected to do. The following rates are per-CRF and based on difficulty of carrying out the PMS:
 - 0 to Pesos 500 – two-page report and/or one follow-up patient visit after the initial consultation; no laboratory work-up needed
 - Pesos 501 to Pesos 1,000 – longer than two-page report, more than one follow-up patient visit after the initial consultation
 - Actual cost of laboratory tests may be reimbursed (invoices must be presented)
 - PHAP will seek expert advice from the PCPM to determine the difficulty level of the PMS study in question.
 - Remuneration must be paid by cheque. Cash is not allowed. Advance payment is also not allowed. Remuneration must be paid after submission and validation of the CRF.
9. PMS enrolment should be limited to 10 patients per doctor per year, i.e., doctors cannot submit and be compensated for more than this number of CRFs per year. The purpose of this limitation is to minimize the chances or the perception of corruption or prescription-buying. For certain disease entities and situations where this rule becomes impractical (such as death of specialist MDs), the company marketing the product may seek an exemption.
10. Violations of PHAP's PMS Guidelines will subject the company to sanctions stipulated in section 18.1.4 of the Code, which defines the type of breach (technical, minor, severe, repetition) and the corresponding fines and penalties. The schedule of penalties is the same as those in "Clinical Trials"
11. These guidelines on the conduct of PMS will be deemed effective immediately upon approval by the Board of Directors of PHAP and notification of all members.
12. Meetings of physicians participating in PMS studies are subject to the same restrictions that apply to clinical investigators meetings (Section 15.0).