National Pharmaceutical Control Bureau (NPCB)
Ministry of Health
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NEWSLETTER OF THE DRUG CONTROL AUTHORITY MALAYSIA

OVERVIEW OF REGULATORY QUALITY CONTROL
Test failures for samples analysed in 1998
Berita Ubat-ubatan June 1999

The role of the Drug Analysis Division of NPCB is primarily to perform analytical tests on pharmaceutical dosage forms in support of the registration program as required by the Control of Drugs and Cosmetics Regulations, 1984 and also the market surveillance program which aims to monitor quality of pharmaceutical products after registration. The samples are tested by the five laboratories of the Laboratory Division namely the Pharmaceutical Chemistry, Pharmaceutical Technology, Pharmaceutical Microbiology, Pharmacology/Toxicology and Traditional Medicines Laboratories.

Assessment of quality, safety and efficacy constitutes an important component of pharmaceutical product evaluation. The acceptance criteria of products subjected to the quality control tests are based on pharmacopoeial, in-house or manufacturer's limits and specifications.

Table 1 lists the minimum general quality control tests for pharmaceutical preparations.

Table 1: Minimum Quality Control Tests For Pharmaceutical Preparations

Types of pharmaceutical preparations	Types of tests
1. Tablet, Capsule, Lozenges	Identification of active ingredient (s) Uniformity of weight Friability Hardness Disintegration Dissolution Moisture content Limit test for degradation products/ impurities Assay of active ingredient (s).
2. Injectable (Liquid)	Identification of active ingredient(s) pH Extractable volume Particle Count Pyrogen / LAL Sterility Effectiveness of microbial preservatives Limit test for degradation products/ impurities Assay of active ingredient (s)
3. Cream, Ointment	Identification of active ingredient (s) Viscosity, Homogeneity, pH, Release rate, Sterility, Microbial limit test Effectiveness of preservatives (if present)

4. Aerosol, Inhalation, Spray	Identification of active ingredient (s) Nett contents Particle size and tests for foreign particles Delivery rate Leak testing Pressure testing Limit test for degradation products/ impurities (where applicable) Moisture determination Assay of active ingredient (s)

The regulation of traditional medicines began in 1992. The evaluation of quality and safety of traditional medicines submitted for registration under phase III also involves laboratory analysis. The minimum requirements imposed on these samples include the following tests:

1. Limit test for Lead, Arsenic and Mercury
2. Disintegration test
3. Microbial limit test
4. Uniformity of weight

The limits set by NPCB for heavy metals are as follows:

- Lead: maximum 10 ppm
- Arsenic: maximum 5 ppm
- Mercury: maximum 0.5 ppm

NPCB has set the limits for microbial contamination as follows:

- Oral Preparations (Non-liquid)

  Bacteria: Not > 5×10^4 per gram
  Fungi: Not > 5×10^2 per gram
  Absence of E. coli, Salmonella, S. aureus and Pseudomonas aeruginosa in 1 gm/ml
  Enterobacteria: Not > 5×10^2 per gm/ml

- Oral Liquid and Topical Preparations

  Bacteria: Not > 5×10^2 per gram
  Fungi: Not > 5×10^2 per gram
  Absence of E.coli, Salmonella,S. aureus and P. aeruginosa and Enterobacteria in 1 gm/ml

For the disintegration test, NPCB has set the following limits for traditional products:

- Capsule/Tablet: maximum 30 minutes
- Sugar coated tablet: maximum 60 minutes
- Pills: maximum 120 minutes

Another quality criteria is uniformity of weight and in this aspect the limits set are:

- Not more than 2 tablets/capsules weighing ± 10% deviation from the average weight.
- No single tablet/capsule weighing ± 20% from the average weight.

Throughout 1998, the Drug Analysis Division tested a total number of 4922 samples with 23,710 tests being performed. Out of these 4922 samples, 366 samples (7.5%), failed the quality control tests. 80% of these samples failed more than one test. Table 2 shows a breakdown of the samples which failed the tests.

Table 2

Category of Samples	ADU	PEN	PMS	TRD	UPF
Sample failed 1 test	2	37	14	208	35
Sample failed 2 tests	0	7	2	28	1
Sample failed 3 tests	0	1	0	0	31
Total number of samples failed	2	45	26	236	67
% Failed (n = 366)	0.5%	12.3%	4.4%	64.5%	18.3%

* Key :

ADU Aduan samples
PEN Samples tested for the purpose of registration
PMS Post market surveillance samples
TRD Traditional samples tested for the purpose of registration and post market surveillance.
UPF Counterfeit Samples from the Pharmacy Enforcement Unit

Table 3

Dosage Form	Tablet	Injection	Galenical	Miscellaneous
Number of samples failed	238	2	109	17
% Failed (n = 366)	65.0%	0.5%	29.8%	4.6%

Table 2 shows that products in the form of tablets and capsules had the highest failure rate. Products in galenical form, which include cream, ointment, syrup, and liquid contributed to 30% of the failed samples. Only a small percentage of injectables failed the test. Preparations such as powders, inhalations, aerosols, patches, medicated soaps, and medicated shampoos were grouped as miscellaneous and this contributed to about 4.6% of the failed samples.

It is also noted that 64.5% of the 366 samples failed the tests were TRD samples. From the pie chart (Figure 1) above, it is shown that 37% of the failed TRD samples were found to be contaminated with mercury, 27% with lead and 9% with arsenic. 5% of the samples failed microbial limit test and the remaining samples either failed the disintegration or uniformity of weight tests.

Figure 2 shows the percentage of PEN and PMS samples that failed the various types of tests. Samples that failed active ingredient tests contribute the highest failure rate for both PEN and PMS samples followed by samples that failed dissolution test, pH and disintegration. Other tests indicated in the above chart include tests for identification, specific gravity, minimum fill, extraction rate and acid neutralizing capacity.

In 1998, the Drug Analysis Division received 1212 samples from the Pharmacy Enforcement Unit, which confirmed that 68 of the samples were counterfeit. 60 of the counterfeit samples subsequently failed tests carried out.

The table below summarizes the results.

Table 4

Names of samples	Number of samples analyzed	Number of samples failed
Tab.Panadol 500mg	17	All samples failed the active ingredient (Paracetamol) test Min: 7.9% Max: 85.0%
Tab.Cortal 80mg	3	All samples failed the active ingredient (Paracetamol) test Min: 41.4% Max: 47.7%
Eye-mo Eye Drops	11	9 samples fail the content of boric acid test. Min: 0% Max: 8.14%
Vicks Vapour Rub	31	All samples failed the content of Eucalyptus Oil, Camphor and Menthol test.