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The Network's NEWSLETTER Rx

Association for Rational Use of Medication in Pakistan

Clinical trials: value and Problems

A clinical trial is done to give definite answer(s) to questions about the management of health problems. A large number of trials tell us nothing of any value because they have been badly designed, poorly done or wrongly analyzed.

Most of the clinical trials done in Pakistan fall in this category. Almost all of them are sponsored by the pharmaceutical industry and most of them are non-randomized, non-controlled and are open. The only idea behind these so called clinical trials is to increase the sale of these drugs.

On the other hand good trials give us important information about one of several treatments used for a particular condition.

In the present issue of the newsletter Professor Andrew Herxheimer has eloquently discussed the ways the clinical trials should be done and what these trials tell us illustrating it with an example from recent literature.

Most of our readers are not familiar with the methodology of clinical trials as nowhere in their medical or pharmacy training are they exposed to it.

A checklist has also been provided which will help in scientific appraisal of clinical trial reports, so diligently passed on to doctors by the representatives of the industry.

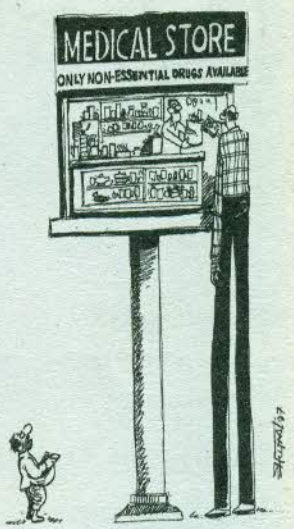
The use of this checklist will reveal that most of these so called clinical trials are worthless and will help the prescribers to critically evaluate the evidence of effectiveness of the products provided by their promoters. This would also help the medical practitioners to make better and rational treatment choices for their patients.

Unquestioned acceptance of the results of clinical trials and then prescribing these drugs in other words mean exposing patients to in-efficacious, dangerous and expensive products.

The Network s mission is to promote rational use of medication and essential drugs concept in Pakistan in order to optimize the usefulness of drugs and help bring equity in their access.

Diminishing essential drugs

While we have been raising concerns regarding the total disregard of the health authorities about non-availability of a large number of essential drugs in the country, there are more and more such drugs going off the shelves, perhaps never to come back again. That is unless there is a drastic change in the present attitude of the authorities and the manufacturers. But these possibilities, we believe, exist only if the sufferers - the people of this country start pressurizing the Government.



The Drug Act 1976 stipulates that "Every drug shall be produced in sufficient quantity so as to ensure its regular and adequate supply in the market". What kind of implementation of law exists in this country and how irresponsible is the drug regulatory which can ensure the availability of essential drugs like Penicillin and Digoxin in the market.

It is quite interesting how this disappearing act typically takes place in the market. First, the company introduces a new "research product" which is priced many times higher with hyperbolic claims and starts promoting it for the same indication side by side with the old product in order to maintain the franchise and goodwill of the prescribers. Once the new product takes root, marketing push for the old product is gradually withdrawn, sales are let to dwindle and the product eventually dies off. Another point of view is that even meager price increases are not approved by the authorities for these essential drugs which even after increase in the price will remain far cheaper than their substitutes.

Few important non-available essential drugs

Phenoxymethylpenicillin
(PenicillinV Syrup®) by Glaxo Welcome is not available in the market for quite some time now.

Digoxin
Cardiac Glycoside by Lahore Chemical & Pharmaceutical Works (Pvt.) Ltd. This life saving drug is absolutely not available.

Thyroxine
by Wellcome for hypothyroidism is not available.

Amitriptyline (Tryptanol®)
by MSD used for agitated depression is also missing.

Phenytoin Sodium (Dilantin®)
by Parke-Davis used for epilepsy is not available.

Niclosamide (Yomesan®)
by Bayer for tapeworm infections is in severe short supply.

Methotrixate
for childhood acute lymphoblastic leukaemia by Lahore Chemical & Pharmaceutical Works (Pvt.) Ltd., Cynamid and Lederle. This important drug is also not openly available in the market and is being black-marketed at a very high cost.

Conditions for registration

1. The Drug(s) must be marketed within 6 months of receipt of this communication.
2. The registration Number, Maximum Retail Price and other particulars shall be provided as per Drugs (Labeling & Packaging) Rules, 1976.
3. Every drug shall be produced in sufficient quantity so as to ensure its regular and adequate supply in the market.
4. The manufacture of any drug shall not, without the prior approval of the Registration Board, be discontinued for a period which may result in its shortage.
5. Colour Scheme of the labels / labeling should not resemble with any of the drug(s) which has / have already been registered.
6. One of the complete method of testing of the finished drugs containing full details of all minor & major steps and protocols alongwith specifications (lower & upper limits) shall be submitted to the following institutions within a period of one month:
   a. Chief Drugs Control & Research Division, National Institute of Health, Islamabad.
   b. Director, Central Drug Laboratory, 7th Street, Defence Housing Society, Karachi.
   c. Director, Drug Testing Laboratory, 1-Birdwood Road Lahore.
7. One copy of the master formula (of all registered drugs) containing the names of active and inactive materials along with the quantities shall be furnished to the Assistant Drugs Controller concerned within a period of one month for which a receipt shall also be obtained.
8. The import of raw materials will be made in accordance with the Import Trade Control Order.

This list of conditions for registration of drugs is from the back page of registration letter provided by MoH to the manufacturer at the the time of registration of the drug!

Chlormezanone - criminal neglect

As mentioned on these pages of the April '97 issue, chlormezanone use has fatal side effects. The leading manufacturer of chlormezanone, Sanofi Winthrop, has been reported by SCRIP (No. 2176, p. 16, 1996), to have decided to withdraw this product worldwide. This withdrawal has taken place in many developed countries including USA since many months now. In France manufacturers of four chlormezanone containing products decided to stop marketing these products in October last year. In fact the clean up action there was so drastic that all the stocks available in the market were immediately recalled by the manufacturer.

This lethal product is still freely available in the Pakistani market in any quantity one may wish to buy. Some brand names of chlormezanone and their manufacturers include: Baserol (Sanofi Withthrop), Muscerol (Pharmatec), and Samerol (Sami).

The Ministry of Health's best response in this regard during the last 3-4 months has been a clarification in the newspapers that a new rule has been made according to which any drug banned in USA, Canada, European Union, Japan, Australia, China, Switzerland or in the country of origin for safety reasons will be banned in Pakistan "automatically". What does "automatically" mean? Has the Ministry de-registered these products, the news report is silent about it. The Ministry's announcement carried by national dailies of April 4 claimed that the concerned companies had already complied with Ministry's directives to refrain from manufacturing and importing this product. Now, the ground reality shows that either the Ministry officials are so naive or else they just do not care a hoot whatever happens to the people of this country. This is potentially a case for suo-moto action by the Supreme Court or Federal Ombudsman. Our past experiences tell us that the MoH will continue to look busy but do nothing in the public interest.

Latest drug registration spree

During a Drug Registration Board Meeting on 16 June 1997 the number of new applications for registration was around a staggering 550 and more than 300 new products were provided registration. How the board members were able to look into the efficacy and safety of these "new products" is any body's guess. Most interesting to know is that the board can also reject applications! How efficient! In the same meeting three new manufacturing licenses were also approved.

Quality assurance drive in the Punjab province: a commendable start

Serious concern has been shown by the Chief Minister , Punjab over the availability of spurious/sub-standard drugs. He has directed the health department to take immediate steps to ensure the delivery of quality drugs to the people. In response, Provincial Quality Control Board in its meeting held on 22nd April 1997, decided to refer the cases of 15 firms who are habitual manufacturer of sub-standard drugs to the Federal MoH with strong recommendations to suspend their manufacturing and registration licenses. These manufacturers have been prosecuted on more than five cases from 1995 to date. We congratulate the provincial authorities on this bold step and expect that the same line will be taken by the Federal MoH. To caution our readers we are producing the name of these dubious manufacturers.

Name of Firm	Total Prosecutions
1. Orient Labs, Lahore	22
2. Iphco International,Lahore	17
3. Flacon Pharma, Gujranwala	15
4. Hydro Pharma, Lahore	19
5. Albro, Lahore	06
6. Anglo Pak, Karachi	09
7. Bentlay Pharmaceutical, Lahore	10
8. Multi Pharama, Lahore	06
9. Cyrus Pharma, Lahore	06
10. Ankaz Pharmex, Karachi	06
11. Venus Pharma, Lahore	09
12. Country Cotton, Lahore	11
13. Shah Brothers, Faisalabad	14
14. Whitesun, Gujranwala	08
15. Warya Brothers, Faisalabad	08