

# **Pre-selection of Traditional Medicine for Clinical Trials in Developing Countries Through the Use of Information and Communication Technology (ICT): A Case Study of South Africa Health Department**

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**KEYWORDS** Clinical. Trials. Traditional. Medicine. Information. Communication. Technology

**ABSTRACT** A high percentage of South African population depends on traditional medicine for treatment but no clinical and scientific validation has been documented in terms of quality, safety, timely and effectiveness of this traditional medicine for treatment. This paper investigated the methods of pre-clinical trials of traditional medicine (herbs) by the health department of North West Province of South Africa. A case study approach was used. Six participants were drawn from an entire population of doctors who are members of the Traditional Medical Council of South Africa and members of Food and Drug Board of South Africa. Data was collected using semi-structured open-ended interview questions to inquire about pre-selection methods for pharmaceutical drugs for clinical trial; pre-selection methods for traditional medicine (herbs) for clinical trial and how effectiveness and the risk factor of any drug is determined. The findings revealed that pre-clinical trial methods are the same for both pharmaceutical drugs and traditional medicine. Both pre-clinical phase use human and animals as subjects of the trial. However participants approached to partake in pre-clinical trial of traditional medicine were reluctant to volunteer because of lack of time, adverse effect of trial on their personal health and uncertainty of Compensation for Occupational Injuries. It became evident that no traditional medicines have been tested on human to be registered with the Medicines Control Council or be prescribed as treatments for any disease in South Africa. The results led to a proposed Pre-clinical Traditional Medicine ICT Framework (PTM-ICT Framework) to collect data on traditional medicine (herbs) directly from the general public and Traditional Medicine Practitioners to ascertain the safety and efficacy of that herb to serve as information needed at pre-selected stage of clinical trial of traditional medicine.

## **INTRODUCTION**

In 1978 at the historic international Conference on Primary Health Care at Alma Ata, the World Health Assembly recommended that governments should give high priority to the incorporation of traditional medical practitioners and birth attendants into the health care stream and proven traditional medicine and remedies into the national drug policies and regulations (World Health Organization-WHO 2002). Despite the dramatic advances and advantages of conventional medicine, it is clear that herbal medicine and traditional medicine plays a critical role in the healthcare sector of many countries. The WHO (2002) indicates that around 80% of the population in Africa use traditional medicines. In sub-Saharan Africa alone there is one traditional healer for every 500 people, whereas there is only one medical doctor for every 40 000 people. Again It has been estimated that 70% of the South African population consult traditional healers for treatment and that the whole industry worth over R250 million (AIDSbuzz 2009). Traditional medicine, has

been defined as practices based on beliefs and ideas to provide health care using herbs and other naturally occurring substances to cure a patient (Conserve Africa 2002). The WHO (2002) further defines traditional medicine as health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and exercises applied singularly or in combination to treat, diagnose and prevent illness or maintain the well-being of an individual. In the last 50 years, humans have relied on plants to treat all manner of illnesses, from minor problems to life-threatening diseases and traditional medicine practitioners (TMPs) claim that traditional medicine play a significant role in the treatment and management of many diseases such as cancers, high blood pressure, cholera, venereal diseases, epilepsy, asthma, eczema, fever, anxiety, depression, benign prostatic hyperplasia, urinary tract infections, gout, and healing of wounds and burns (Helwig 2010). Despite the wide claim by TMPs in South Africa, no adequate scientific validation has been documented in terms of quality, safety, timely

and effectiveness of the herbs use for treatment to contribute to primary health care practices in the country. However the use of ICT can aid the provision of scientific evidence regarding the safety and effectiveness of the herbs use by TMPs through pre-selection of traditional medicine for clinical trial. Clinical trials on one hand are sets of tests in medical research and drug development that confirms the safety and efficacy of a drug. This test provides information about adverse effects and reactions of the drug for health interventions. Before clinical trials are conducted, satisfactory information has to be gathered on the safety of the drug through non-clinical method and has to be approved by the health authority in that country. This non-clinical trials which is referred to as pre-clinical trials are conducted using human and animal as subjects. In this research clinical trial is defined as the testing of herbal plants in the treatment of specified diseases.

### Objectives

This research therefore investigated the methods of pre-clinical trials of traditional medicine (herbs) by the health department of North West Province of South Africa and based on the findings propose an ICT framework to aid pre-selection of traditional medicine for clinical trial. The rest of the paper is presented as follows: related work, methods, results and discussion and a proposed ICT framework.

### Related Work

Traditional medicine can supplement the provision of primary health care in South Africa. Current estimates suggest that, in many developing countries including South Africa, large proportion of the population relies heavily on traditional medical practitioners and medicinal plants to meet their primary health care needs (NRCATM 2010). Although modern medicine may be available in these countries, herbal medicines have often maintained popularity for historical and cultural reasons. Therefore traditional medicine continues to play a significant role in the treatment and management of many diseases such as cancers, high blood pressure, cholera, venereal diseases, epilepsy, asthma, eczema, fever, anxiety, depression, be-

nign prostatic hyperplasia, urinary tract infections, gout, and healing of wounds and burns in South Africa (Helwig 2010). Traditional medicine, has been defined as practices based on beliefs and ideas to provide health care using herbs and other naturally occurring substances (Conserve Africa 2002).

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions (including drugs) to evaluate the effects on health outcomes (WHO 2002). Drug trial on humans starts with pre-clinical stage which is also named as nonclinical studies and it is very important stage of the test. Pre-clinical (initial test in humans) stage begins before the actual clinical trials begins, and during that stage important feasibility, iterative testing and drug safety data is collected. Clinical trials involving new drugs are commonly classified into five phases. Each phase of the process is treated as a separate clinical trial. The drug-development process will normally proceed through all five phases over many years. If the drug successfully passes through Phases 0, 1, 2, 3 and 4, it will usually be approved by the national regulatory authority for use in the general population. Each phase has a different purpose and helps scientists answer a different question:

In Phase 0, trials is called pre-clinical phase and is the first-in-human trials. Single sub therapeutic doses of the study drug are given to a small number of subjects, humans or animals (10 to 15) to gather preliminary data on the drug's pharmacodynamics (what the drug does to the body) pharmacokinetics (what the body does to the drugs) and toxicity testing (Craig and Walter 2000).

In Phase 1 trials, researchers test an experimental drug or treatment in a small group of people (20-80) for the first time to evaluate its safety, determine a safe dosage range, and identify side effects. In Phase 2 trials, the experimental treatment is given to a larger group of people (100-300) to see if it is effective and to further evaluate its safety. In Phase 3 trials, the treatment is given to large groups of people (1,000-3,000) to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow it to be used safely. In Phase 4 trials, post marketing studies delineate additional informa-

tion, including the treatment's risks, benefits, and optimal use.

Before any health organization or pharmaceutical companies start clinical trials on a drug, they conduct extensive preclinical studies which Information and Communication Technology has the potential of keeping information on medicinal plant, its effectiveness and safety for human use at preclinical stage before actual clinical trial commences. Current information can be collected from the public who use traditional medicine and traditional medicine Practitioners (TMPs) through ICT. These set of information can be integrated by the use of ICT for analysis. Arzt (2007) indicates that there are different ICT models of interoperability which an organization can adopt, the Centralized Model, the Co-operative Model and the Distributed Model.

A Centralized Model utilizes a centralized server where the records of all the patients are registered, matched, and de-duplicated. Data may be collected from various sources behind the scenes, but users may only access a single consolidated application or suite of applications. Due to the fact that the data and the applications are more centralized, data security tends to be more straightforward.

On the other hand a Co-operative Model is a combination of the Centralized and the Distributed Models. It has both a central storage and a mechanism for obtaining data from participating servers on demand. The advantage of the Co-operative Model is that, data is stored centrally and what remains distributed can be anywhere between 0 and 100 percent of data. In the Centralized Model, data that is not in the central storage can never be available to subsidiary servers. Similarly, in the Distributed Model, no data can be obtained. The recognition of health ICT is not an end unto itself but a means to an end, which is a better quality, safer, more value-driven and accessible healthcare information to all people (E-health Initiative 2008: 2) both present and future.

## METHODS

The research study was conducted in three rural communities, Taung Ganyesa and Christiana in the Bophirima Region of the North West Province in South Africa. These three communities were selected because they are purely traditional set up communities which are governed by traditional chiefs and strongly rooted in the usage of traditional medicine in South Africa.

Given the nature of the study, a case study approach provided the most effective method for data collection. Participants for the study were drawn from an entire population of Doctors who are members of the Traditional Medical Council of South Africa and members of Food and Drug Board of South Africa. Six doctors were selected based on their affiliation with the South Africa Traditional Medical Council and Food and Drug Board of South Africa as well as a practicing in rural community. In describing population, Polit and Beck (2008) indicate that it is the aggregate of cases having a common and designated criterion that is accessible as subjects for a study. A purposive sampling technique was used in selecting the participants. Two doctors from each community hospital were selected making a total of six doctors from three communities. All the six doctors voluntarily agreed to take part in the study. Table 1 indicates the number of participants according to their professional category, sex and age.

Data was collected using semi-structured open ended interviews. This data collection method was used because a structured interview does not allow flexibility to explore interesting issues that arise, and an unstructured interview does not provide enough focus. Therefore a semi-structured interview was used. The interviewees represented different roles ranging from specialist doctors to non-specialist doctors. The interviewees were asked to tell in their own words:

**Table 1: Participants demographics**

| <i>Professional category</i>           | <i>Number selected from Communities</i> |                |                   | <i>Sex</i>        | <i>Ave Age</i> |
|----------------------------------------|-----------------------------------------|----------------|-------------------|-------------------|----------------|
|                                        | <i>Taung</i>                            | <i>Ganyesa</i> | <i>Christiana</i> |                   |                |
| Specialist doctors                     | 1                                       | 1              | 1                 | 3 males           | +45            |
| Non-specialist (General practitioners) | 1                                       | 1              | 1                 | 2 males; 1 female | +25            |
| Total                                  | 2                                       | 2              | 2                 | N=6               |                |

- How they pre-select pharmaceutical drugs for clinical trial.
- How they select traditional medicine(herbs) for clinical trial
- How they determine the effectiveness and the risk factor of the drug

Integrity of data entry from the study was checked by another researcher. Transcripts were coded using Wolcott's (1994) methods of case study analysis techniques. After the initial coding, broad categories were identified by searching for patterns in the participants' responses. Four categories were identified and discussed in the results and discussion section below.

## RESULTS AND DISCUSSION

The main purpose of the research paper was to investigate the methods of pre-clinical trials of traditional drugs (herbs) by the health department of North West Province of South Africa and based on the findings propose an ICT framework to aid pre-selection of traditional medicine for clinical trial. The findings and discussion are summarized under the following headings; pre-selection of pharmaceutical drugs for clinical trial, selection of traditional medicine (herbs) for clinical trial and determination of the effectiveness and the risk factor of the drugs. Each of these headings is discussed in detail in the following paragraphs.

### Pre-selection of Pharmaceutical Drugs for Clinical Trial

The respondents indicated that before a clinical trial is undertaken for any drug, the trial information is required by the South African National Clinical Trials Register for approval. This constitutes an initial ethics application process and the trialists initially capture trial details on-line. A proof of capture form is printed and submitted with the ethics application pack to the relevant accredited research ethics committee for that trial to proceed.

Again the respondents indicated that before a trial is initiated, all, foreseeable risks and inconveniences are weighed against the anticipated benefit for the individual trial subject and society. A trial is initiated and continued only if the anticipated benefits justify the risks. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science.

Two doctors stated that, "*new medicines are studied in great detail over a long period, in the laboratory and in various animals to establish its initial safety and effectiveness. Trials or testing of medicines and/or devices in people only takes place after they have been tested thoroughly in the laboratory on animal studies*". The testing of investigational (new) drugs, vaccines and medical devices in humans usually follows a process that can be broken up into four phases or steps.

During this first phase a new drug, vaccine or medical device is tested in a small group of usually healthy persons for the very first time. In the Phase 1 clinical trials the aims are to determine the general safety, the correct dosage and possible negative or undesirable effects of the new drug, vaccine or medical device.

In Phase 2, clinical trials the new drug, vaccine or medical device is tested in a larger group (several hundred healthy people). At this stage people with the disease for which the new drug, vaccine or medical device is developed are also given the opportunity to participate in testing it. The purpose of Phase 2 is to further test the safety and effectiveness of the new drug, vaccine or medical device.

In Phase 3, as indicated by the respondents, the new drug, vaccine or medical device is tested in a larger group of people who suffer from the disease/illness for which the new drug, vaccine or medical device is intended. The effectiveness and possible undesirable effects are evaluated in more depth during this phase. The new drug, vaccine or medical device is compared to old registered (licensed) drugs, vaccines or medical devices, or alternative treatment options.

During Phase 4 the drug, vaccine or medical device is tested in several thousands of people to: define its safety, effectiveness, long-term undesirable effects, test the new drug, vaccine or medical device in certain high risk sectors of the population like children, the elderly, people with liver and kidney diseases, and find new uses (indications) of the new drug, vaccine or medical device. In phase four, the new drug, vaccine or medical device is registered and licensed for sale by the Medicines Control Council (MCC).

Phase 1 as described by the respondents corresponds with the pre-clinical activities (Pharmacodynamics and Pharmacokinetics) as indicated by (Craig and Walter 2000). At this stage,

human subjects are used and it is very difficult to get volunteers to partake in such trials because of the many disadvantages associated with the use of human subjects. Some of these disadvantages indicated by Shayne (2009) include:

- People setting aside time for trial related activities like visiting the trial site which affects their daily routine
- Individual's private or social life may be affected, for example, sexual activity, reproductive functioning, consumption of alcohol, tobacco and other drugs of abuse.
- Participants in the trial may have their employer, medical aid, personal insurance and/or Commissioner for Compensation for Occupational Injuries not paying for claims that are related to events due to your participation in clinical trials.

These disadvantages do not only affect the individual participants who may volunteer to partake in the trial but also hamper the initial or preclinical activities in clinical trial of new drugs.

#### **Pre-selection of Traditional Medicine for Clinical Trial**

The respondents indicated that there are four stages in testing medicines including traditional medicines before they can be registered with the Medicines Control Council as treatments for any diseases. The first stage is to test that the traditional medicine is not harmful to animals or human cells.

- A Phase 1 human trial involves a relatively small number of healthy human volunteers in order to test the herb for possible side effects. However people are usually not ready to participate in the first phase because of fear of uncertainty about the safety and effectiveness of the herb.
- A Phase 2 trial involves about 200-500 human volunteers with the disease and tests for safety and an indication of a positive immune system response. This phase also tries to determine the optimal dosage.
- A Phase 3 trial involves several thousand human volunteers with the disease and assesses whether the herb has any positive effects on disease progression. This type of trial is called a double-blind, placebo-controlled trial and is considered the gold standard in measuring the efficacy of a medicine.

All three phases usually make use of placebo groups. This means that some of the participants will receive a harmless substance that looks like the herb being tested but does not contain any active substance. The 'placebo' group is then compared with the group that received the actual test herb. This is important to show that it is the herbal treatment that is making people feel better. Some people feel better simply by believing that they are taking a strong medicine. This is called the placebo effect and it is accounted for in all human trials because it is so strong. On average 30% of people will feel better after taking a placebo medicine. No African traditional medicines have yet been tested with any Phase 3 human trials, and therefore cannot be registered with the Medicines Control Council or be prescribed as treatments for a specific disease.

No African traditional medicines have yet been tested with any Phase 3 human trials, and therefore cannot be registered with the Medicines Control Council or be prescribed as treatments for any disease.

The preclinical phase of testing of traditional medicine possesses a great challenge to participants because of the uncertainty of the harmful effect of the herb. This uncertainty will prevent many people to volunteer to partake in the trial. However, traditional medicine practitioners as well as the patients who consult these TMPs claim the positive effect of the traditional medicine they use. This is confirmed by the WHO (1995) that around 80% of the population in Africa use traditional medicines. In sub-Saharan Africa there is one traditional healer for every 500 people, whereas there is only one medical doctor for every 40 000 people. Again It has been estimated that 70% of the South African population consult traditional healers and that the whole industry is worth well over R250 million. The question is how can ICT framework be developed to gather information on different herbal medicine from the population to serve as a source of preclinical testing for different traditional medicine? In answering the question the researcher propose an ICT framework to aid pre-selection of traditional medicine for clinical trial.

#### **The Effectiveness and the Risk Factor of the Drugs**

The respondents indicated that the effectiveness and the risk factor of the drug, (being it a

traditional medicine or not) is determined greatly at the pre-clinical stage where human and animals are given the drug to observe if the drug is harmful to animals or human cells. “*We make use of placebo groups*”. This means that some of the participants will receive harmless substance that looks like the herb being tested but does not contain any active substance. The ‘placebo’ group is then compared with the group that received the actual test herb. This is important to show that it is the herbal treatment that is making people feel better. Some people feel better simply by believing that they are taking a strong medicine. This is called the placebo effect and needs to be accounted for in all human trials because it is so strong. On average 30% of people will feel better after taking a placebo medicine. Three respondents stated that “*No African traditional medicines have yet been tested with all the phases in human trials, to be registered with the Medicines Control Council or be prescribed as treatments for of any disease in South Africa*”.

### The Need for ICT Framework

Based on these findings the researcher proposes a Pre-clinical Traditional Medicine ICT Framework (PTM-ICT Framework) as indicated

in (Fig. 1). The purpose of this framework is to collect data on traditional medicine (herbs) directly from the general public and Traditional Medicine Practitioners to ascertain the safety and efficacy of the herb to serve as traditional medicine for clinical stage trial. This means the PTM-ICT will discover the eligibility of the traditional medicine for clinical trial. First it will acquire information about the herb from traditional medicine users. Secondly it will acquire information about the herb from TMPs. The PTM-ICT will then link and compare the two sets of data and based on eligibility criteria, select the traditional medicine for clinical trial. This will prevent recruiting participants (human and animal) as subjects for pre-clinical trials.

The (PTM-ICT Framework) has an acquisition face, archiving and quality control face, and dissemination, processing and analysis face. The acquisition face has a user interface component which allows the public to register and indicate diseases which they once suffered from and write the name of the traditional medicine or herb which helped to cure the disease. The user interface will also allow TMPs to register a traditional medicine (herb) which they used to cure certain disease. The subsequent paragraphs de-

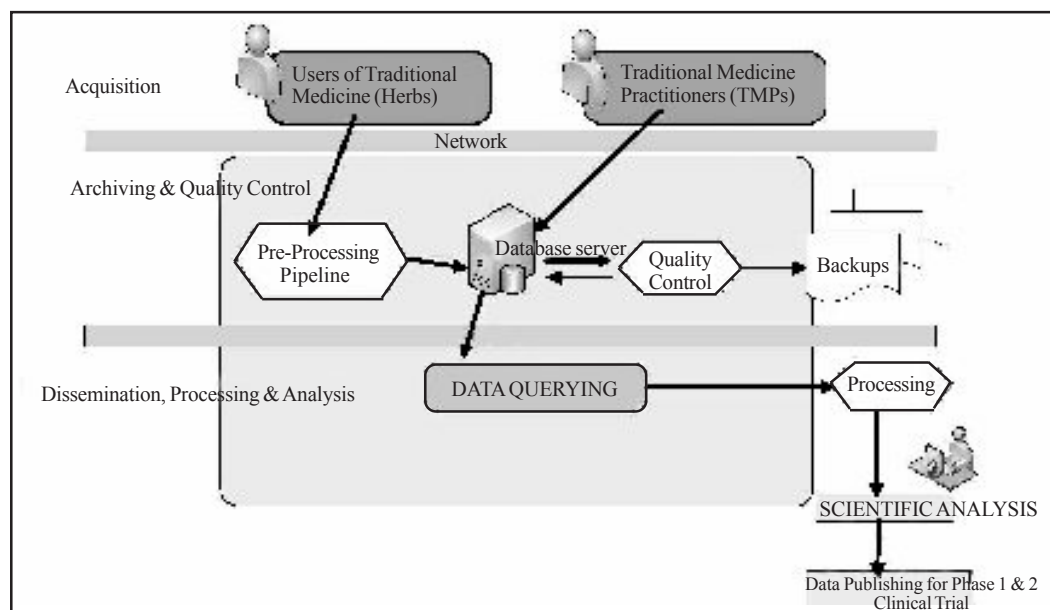


Fig. 1. The PTM-ICT framework

## Dissemination, Processing and Analysis Face

This is a uniform data integration architecture that provides consistent support to scientific analysis. The integrated data ensure interoperability between data received from TMPs systems and traditional medicine users system. These data are linked, processed and analyzed for publication in traditional medicines register indicating which traditional medicine are frequently used and safe for clinical trial.

The interaction between components across the different layers in the PTM-ICT Framework is supported by an appropriate transport protocol, such as HTTP for Internet communication and TCP for intranet communication and is considered for sending messages. All the components of the PTM-ICT Framework communicate through a shared network infrastructure using an agreed service protocol. An HL7 messaging standard has been adopted as the messaging standards for the healthcare sector in South Africa. However, there are plans to move to an XML based standards for messaging requirements. Therefore, the PTM-ICT Framework adopts these national messaging standards.

## CONCLUSION

Having reviewed the problems associated with pre-clinical trial of traditional medicine (herbs), unpacked the role of traditional medicine and the phases of clinical trial of drugs, it was noted that traditional medicine seldom go for clinical trial. However the few traditional medicine which are taken for clinical trial are

**Table 2: Diseases categorization**

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                  |                                   |                                 |                     |                                |                            |                        |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|-----------------------------------|---------------------------------|---------------------|--------------------------------|----------------------------|------------------------|
| <a href="#">Home</a>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | <a href="#">Userregistration</a> | <a href="#">TMPs registration</a> | <a href="#">Type of disease</a> | <a href="#">FAQ</a> | <a href="#">Capture trials</a> | <a href="#">Contact us</a> | <a href="#">Log in</a> |
| <div> <a href="#">Select a disease</a> <a href="#">Disease heading</a> <a href="#">Name of traditional medicine (herb) which cured the disease</a> <a href="#">Number of times used</a> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                  |                                   |                                 |                     |                                |                            |                        |
| <ul style="list-style-type: none"> <li>○ Bacterial and fungal diseases</li> <li>○ Behaviors and mental disorders</li> <li>○ Blood and lymph conditions</li> <li>○ Cancers and other neoplasms</li> <li>○ Conditions of the urinary tract and sexual organs, and pregnancy</li> <li>○ Digestive system diseases</li> <li>○ Diseases and abnormalities at or before birth</li> <li>○ Ear, nose and throat diseases</li> <li>○ Eye diseases</li> <li>○ Gland and hormone related diseases</li> <li>○ Heart and blood vessel diseases</li> <li>○ Immune system diseases</li> <li>○ Injuries, poisonings, and occupational diseases</li> </ul> |                                  |                                   |                                 |                     |                                |                            |                        |

first tested at pre-clinical stage using human and animals as subjects. This constituted a huge problem due to lack of volunteers. Volunteers participating in the trial are always not willing because of uncertainties regarding the safety, efficiency and effectiveness of the traditional medicine. This problem has prevented any traditional medicine in South Africa to be tested through all the phases of clinical trial. Therefore no traditional medicine has been registered with the Medicines Control Council of South Africa to be prescribed as treatments for a specific disease.

The results of the research led to the proposal of PTM-ICT framework to aid with the collection of data on traditional medicine (herbs) directly from the general public and traditional medicine practitioners to ascertain the safety and efficacy of the herb to serve as pre-clinical stage of the trial of traditional medicine.

## RECOMMENDATIONS

Based on the findings it is recommended that the proposed PTM-ICT framework be implemented on a pilot scale in the North West Province of South Africa. The pilot implementation should take into account the installation of a broader internet bandwidth to improve internet connectivity and speed of the Public Internet Terminals (PIT) in rural communities in South Africa.

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