Understanding clinical trials and their outcomes – fake science at its best!

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The term clinical trial is often used in the scientific literature and recently more so in the public media regarding developing treatments (e.g., pharmaceutical products, vaccines) for COVID-19 and its associated pandemic. The term clinical trial is often presented to the public as a highly sophisticated science-based approach for developing medicines and treatments. Further, it has been implied that clinical trials require a higher level of understanding of the complexities of science and financial recourses, which presumably only a few developed economies can afford and support. The purpose of this article is to decipher the mystery of clinical trials in simple language so that the public could understand them and provide guidance to the professionals in the area.

In simple terms, a clinical trial is a form of testing or test where tests are conducted using humans as test subjects for the development of medicines, whether tablets/capsules or vaccines. If the same testing is conducted in animals, it is called pre-clinical, otherwise in vitro, or laboratory testing (i.e., without dosing humans or animal subjects). A simple example of a "clinical trial" would be a trial/test to see if one gains weight (the outcome parameter) by eating chocolate loaded ice-cream for a month. Such a trial/test can easily be done at home by anyone. What would be required for such a clinical trial is chocolate loaded ice-cream, some human subjects, and a weighing scale to monitor the weight (outcome or response parameter) before and after taking the ice cream (or the so-called "dose").

The point, which must be kept in mind, is that a clinical trial is testing to monitor or measure outcome (response) before and after the treatment ("dose"). This means that clinical trials should be conducted under normal/standard analytical (measurement) science or laboratory management. If the test products are chemical-based (simple or complex), tests should be conducted in an analytical chemistry laboratory. However, a quick overview of the literature would reveal that most, if not all, clinical trials are conducted under non-analytical chemistry management, mostly having medical, pharmaceutical, and regulatory expertise. These professions usually have no or limited underlying and required knowledge or understanding of analytical science and/or chemistry of the tested products and/or chemical nature of the body processes. Therefore, it would be safe to assume that most "clinical trials" conducted at present would be of low scientific authenticity, more likely false, and useless.

Current practices may be explained by evaluating pharmaceutical products such as tablets or capsules. However, it can further be made simpler to understand by considering an example of developing a generic product vs an innovator product.

The idea behind such evaluation is to establish if the generic products are of the same or similar

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quality, safety, and efficacy as those of the respective innovators' products. To demonstrate this, one is required to conduct clinical trials, commonly known as bioavailability and/or bioequivalence assessment, for comparing a generic product against an innovator's product. That is to conduct testing after dosing the two products separately and measuring and comparing the outcome (response), which in this case is the drug levels of the administered drug. For example, suppose someone likes to develop a generic version of Tylenol or Advil. In that case, he/she has to administer a Tylenol or Advil against the tablet's in-house version and measure the plasma drug levels, which would be acetaminophen or ibuprofen, respectively. Input is a tablet, innovator, or generic, and output is plasma drug levels - basically a standard or typical analytical chemistry protocol. However, such studies are conducted under the management of medical and pharmaceutical professionals following regulatory guidance with negligible contribution from chemical and/or analytical sciences for developing study protocol and/or interpretation of the results.

An appropriate analogy to describe the situation or testing would be assessing the comparative efficiency of new fuel vs. the old one for ships. Ships would be operated following normal or standard protocol without knowing about the tested fuel manufacturing and testing aspects. The ship will be loaded with new or old fuel at random and will be operated as usual, and at the end, fuel consumption is measured and evaluated without the involvement of ship caption or crew. If the fuel loader and ship operators kept blinded about which ship is getting which fuel, the testing/evaluation will be called double-blinded in technical terms.

Similarly, if two medicinal products are to be tested in a double-blinded "clinical trial," both product administrators and volunteers would be blinded to the tested products. A medical practitioner's role would be just like a ship captain to "operate" and monitor the normality of the patients or volunteers. A medical/pharmaceutical practitioner would have no or limited knowledge about the manufacturing and/or quality of the products tested and/or their evaluation.

Now let us explore the product evaluation in little further detail. The input part is the tablets or capsules, which are compressed composite of the drug and some inactive ingredients for all practical purposes. This is similar to a candy-making process (consider M&M candy) and note that it happens before the tablets/capsules are part of clinical testing. No matter how loudly an argument is made, the fact remains that it is a chemical composite or candy manufacturing process. Chemical and/or physical tests are conducted to establish the tablet/capsule products' suitability before administering to human subjects. Once the product is administered, blood samples are withdrawn from human subjects to measure drug levels again in a typical analytical chemistry laboratory or environment. The blood drug levels are compared to establish the two tested products' similarity following standard analytical chemistry and statistical principles and methods.

Now consider if indeed, one is measuring and/or evaluating the similarity of the two tested products. One would measure the mean and variability (variance) of blood drug levels for these two products in scientific or technical terms. If the

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means and variabilities are similar for both products, then the products will be declared equivalent, and authorities would allow their interchangeability. However, the question is, is this comparative protocol valid for seeing the mean and variability similarity or differences in the compared products? The answer is certainly no! The reason is, for such a protocol, there are three sets of variabilities contributing to the blood drug levels, i.e. (1) inter and intra-products (tablets/capsules); (2) inter and intra-human subjects - physiological; (3) blood drug level measurements. It is well-known that most variability in this regard comes from human physiological variations, which are extremely high and impossible to control or reduce. Products and drug measurement variabilities are usually small and insignificant and are buried (confounded) in the physiological variability. Therefore, it is impossible to accurately determine the variabilities of the products or their quality, which is the main objective of conducting the bioequivalence assessment or the so-called clinical trials. It is often assumed that statistical analysis of the data takes care of the different variabilities aspects. However, unfortunately, this is not an accurate assumption as statistical analysis presumes constant or fixed intra- and inter-subject variability - which is not correct. So what is the use of conducting such testing/clinical trails – not much! It is important to note that such clinical trials are conducted not only for developing generic products but also for innovators' products. Every time a product is developed, the authorities require such bioavailability assessments of the drugs in humans and are conducted accordingly.

In short, such studies (clinical trials) are not only scientifically false for the intended purpose but also falsely assure the public that products are being assessed and approved based on science and/or clinical assessment. Furthermore, unfortunately, participating human subjects, most healthy adults, are exposed to unnecessary risk of potent chemicals labeled as "lifesaving medicines."

Now let us consider the recent vaccine development aspect with the above-described clinical trial explanation for assessing a vaccine's safety, efficacy, and quality and/or its product. Conducting a study/testing/clinical trial, as noted above, one is required an input (dose of a vaccine), output (response), and human (patients or healthy subjects treated with the virus). Concerning the vaccine dose, the question is, where will this vaccine candidate come from to initiate a clinical trial? The only way a trial vaccine could be developed is if one has access to a virus that the potential vaccine candidate would be capable of killing, at least in vitro. However, it is well-known that a reference virus (identified and quantified) is not available in sufficient quantities. It is then how a potential vaccine candidate would be developed to administer for clinical trials. It cannot be! Therefore, having an appropriate vaccine candidate to conduct clinical trials is impossible.

Let us assume that, magically, a potential vaccine candidate becomes available and ready for dosing to the subjects. Then after dosing, what would be the measurable response that one would be monitoring to establish the vaccine's efficacy – presumably immunity to the virus and/or its infection? The only way to know about immunity would be to inject the virus to create sickness to see if the created immunity kills the virus and/or protect humans from the illness. However, as

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stated previously, there is no virus SARS-COV-2 available hence immunity against the virus cannot be checked and/or established. So, what would these clinical trials be for – obviously, nothing! Scientifically speaking, conducting such clinical trials is simply futile, at least at present. However, medical, pharmaceutical and regulatory professionals promote and conduct clinical trials while exposing human subjects to potentially dangerous and potent chemicals. Therefore, the so-called "science" of clinical trials should be challenged for its lack of relevance and usefulness on an urgent basis.

Currently, medical and pharmaceutical science works based on regulatory compliance, which means meeting regulatory criteria set mostly with arbitrary or fictional standards and specifications, at least from a scientific perspective. For example, the compliance requirements of bioavailability/bioequivalence assessment are purely on an arbitrary basis, as explained above, which does not provide any assurance about the tested products' quality, safety, and efficacy. However, authorities would approve the products as safe and efficacious because they (products) meet their (authorities') compliance criteria.

Similarly, in vaccine development, there is no possibility of developing an appropriate and valid vaccine as neither a valid reference virus nor a valid test is available to monitor the vaccine's efficacy. On the other hand, authorities would set some arbitrary compliance requirements/standards based on RNA/DNA monitoring and some antibody testing, both mostly nonspecific and irrelevant, as described previously. Therefore, if a vaccine is developed, it will not be assessed and approved based on its killing or neutralizing ability of the virus or curing patients but based on meeting regulatory compliance requirements mostly unrelated to the virus and/or its associated disease (COVID-19).

On the other hand, if one considers the issue based on analytical or measurement science, the problems can be resolved accurately, with extreme efficiency, and cost-effectively.

For example, in the case of bioequivalence testing, such irrelevant and flawed clinical testing is not necessary and should be discontinued immediately from the regulatory requirements. The products' quality, efficacy, and safety (generic and innovators) can easily, accurately, and scientific validity can be established with laboratory testing alone. In this regard, it is hard to argue against using valid laboratory-based testing alone.

As explained above, not only is it impossible to develop an appropriate and valid vaccine, but it is not even necessary to develop one. At least two issues to consider in this respect are: (1) presumably, vaccines are being developed for a still unknown or non-quantifiable virus, so chances of success are almost zero; (2) vaccine is being developed for protection/immunity from future viral attack. Therefore, what are the chances of returning to exactly the same virus in the future – low to zero? Arguably, experts in virology and epidemiology mistakenly claimed ownership of the situation, resulting in a fake viral pandemic with a suggested solution to develop and have a vaccine. However, the issue belongs to analytical science and chemistry.

Suppose one considers that the world has been attacked by a virus that causes severe acute respiratory syndrome (SARS), resulting in

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infection, which may lead to serious health issues and possibly deaths. Hence logically, would it not be more appropriate to treat the infection with typical infection medicines such as antibiotics? There are suggestions that SARS infections can be treated with antibiotics. However, such treatment is neither allowed nor encouraged for unknown reasons. Suppose, for some reason, it is considered that an improved and/or specific antibiotic is needed. In that case, developing a new or modified antibiotic will be much more efficient and cost-effective. The reason is that the dose (input) would be a defined and well-characterized chemical compound (antibiotic) relatively easier to develop and manufacture in large quantities with defined characteristics, and output or response would be measurable, i.e., changes in infection levels. However, there appears to be a clear mindset that the only solution is a vaccine that needs to be developed. Such an approach certainly lacks logic indicating the practice of flawed or fake science. This also suggests that the disease/pandemic and its treatment are in the wrong hands, unfortunately with false assumptions and criteria, because claims are being made for virus and developing vaccines when trials or studies are about analytical chemistry or science.

In summary, clinical trials are a specific type of test in which products or treatments are tested using human subjects. Such trials should be conducted under analytical science or laboratory management with scientifically valid protocols. Unfortunately, trials are conducted in non-analytical science facilities and supervision, often with invalid study protocols and interpretations. Approved products based on such trials would provide false assurance of the tested products' safety, efficacy, and quality. Patients and the public should be aware of current flawed scientific practices in this regard. On the other hand, if such evaluations are conducted with appropriate, scientifically valid, and proven approaches, one could avoid false mishaps and develop treatments and cure far more expeditiously and cost-effectively.

PS: If one requires specific references to the views presented here, they could be obtained by visiting the site (https://bioanalyticx.com/) or directly contacting the author at principal@pharmacomechanics.com.

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