Science at the authorities – deceptive and fraudulent!

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Regulatory authorities, in particular FDA/CDER, often hold workshops to guide the industry in developing pharmaceuticals or medicines considering underlying scientific principles. However, a critical overview here highlights the falseness of science.

FDA /CDER often conducts workshops guiding the industry to assist in drug development approaches so that the approval of their drug applications goes smoothly and expeditiously.

A recent example of such a workshop is "Advancing Generic Drug Development, Translating Science to Approval" (link).

This workshop is to help the industry and small businesses whose sole business is manufacturing drug products by the "experts" at FDA who never manufacture any drug product. So how does it make sense? It does not! Therefore, understandably, FDA and worldwide authorities make bizarre and glaringly stupid mistakes in "guiding" and "helping" the industry.

The workshop title, "Advancing Generic Drug Development," is scientifically incorrect because there cannot be a "generic drug." Generics are always "drug products." For example, acetaminophen is a drug (a pure chemical compound). However, Tylenol is a product, a composite of chemicals, including acetaminophen. Different manufacturers can manufacture acetaminophen products, but they all must have the same drug (acetaminophen). However, for some mysterious reasons, in fact, in ignorance, medical and pharmaceutical experts do not see this difference.

Scientifically, manufacturing both (drug and drug products) is a part of the chemical industry. In most cases, drugs can be purchased from chemical manufacturers or distributors with the same or better quality attributes as required by the FDA or local or national authorities. However, drug products, even though they are composite of chemicals, often thoroughly investigated, and are manufactured based on chemistry principles and methods, cannot be purchased from chemical manufacturers. This is because authorities prohibit the chemical industry from selling. Instead, they can only be obtained from still chemical manufacturers but approved by the authorities, which label them pharmaceutical manufacturers.

In short, a pharmaceutical manufacturer is a chemical manufacturer. The labeling and approval of pharmaceutical manufacturing are done by authorities dominated by experts, mainly physicians and pharmacists. Therefore, a chemical manufacturing plant becomes a pharmaceutical plant by getting "approval" from physicians and pharmacists.

I hope people see here the anomaly that physicians and pharmacists are guiding the development and manufacturing of chemical products. However, these professionals do not study or are trained in the chemistry/science aspect of these products/pharmaceuticals. Instead, they are trained to suggest (use or

prescribe) and administer the pharmaceuticals. They are the users of chemical compounds and products. Please consider studying the curriculum of medical and pharmacy degree programs.

It is like a chef uses farm products to prepare dishes. A chef uses and knows about vegetables, meat, and dairy items but is not expert or knowledgeable in producing ("manufacturing") the farms' items, let alone guiding the farmers on how to create/develop the farm items.

On the other hand, modern-day physicians and pharmacists (chemical users) are considered and promoted as experts in chemical development and manufacturing, mainly by health authorities and news media around the world.

The even more bizarre thing is that these medical and pharmacy experts are also promoted as scientists when, in reality, they never have studied or trained in science or conducted relevant scientific experimentation. Please consider looking at any curriculum for such degree programs (e.g., link)

Now let's consider the topics discussed during the workshop (link).

"TOPICS COVERED

- *Peptide and Oligonucleotide Active Pharmaceutical Ingredient (API) Sameness and Impurity Assessment Considerations*
- *Drug-Device Combination Products*
- *Long-Acting Injectables*
- *Oral Complex Drug Products*
- *Nasally Administered Products*
- *Quantitative Methods and Model-Integrated Bioequivalence Approaches*
- *Suitability Petitions"*

Technically and scientifically, most, if not all, relate to **testing** the **drug products**, not the drug development, as noted in the workshop title, i.e., testing chemical compounds/products. Testing is conducted following (FDA and other similar regulatory authorities) in-house developed protocols called guidelines or guidance documents.

From a medical products perspective, the two most common testing approaches are: (1) in vitro or drug dissolution testing and; (2) In vivo or bioequivalence (BE) testing. BE testing is sometimes referred to as clinical testing or trials.

In vitro or drug dissolution testing is based on measuring drug release from its product within a round-shaped beaker with a stirrer called a drug dissolution tester or apparatus (see here). It is a well-established regulatory requirement for a drug product to be approved for marketing. A more detailed description of the technique, its scientific basis, and its applications may be found here (link).

However, unfortunately, the technique has not been validated (authenticated) for its use, i.e., it has not been shown that the technique or tester can produce relevant and valid

dissolution results. In fact, considering the physical limitations of the testers, they cannot provide valid and relevant results (link).

In a recent response to the Citizen Petition for withdrawing the use of the non-validated dissolution testers, while acknowledging the invalidity of the testers, FDA rejected the petition describing that the tester becomes validated when one tests the products following in-house developed guidelines (link). Note the in-house developed guidelines are based on these invalid testers. A test product (a product under development) cannot be used to validate a test. Using a test product to validate the tester is illogical and unscientific. It confirms that experts have no idea of the fundamental principles and requirements of science, establishing that experts at the FDA cannot be considered scientists.

In scientific terms and following FDA's cGMP (Current Good Manufacturing Practices) Guidelines, using invalid tests or testers is considered a deceptive practice punishable by law and its own (FDA) rules and guidelines (link). However, FDA arrogantly enforces the guidelines as science-based. No one would make such a claim or enforce such a policy if they had studied science to any degree. Therefore, all claims by the FDA and other regulatory authorities about the product assessments must be considered false and fraudulent.

On the other hand, FDA and regulatory agencies, particularly in developed countries, defend their product assessment and approval claims based on the second test, the BE test.

First, this test is not conducted on products that consumers/patients use, i.e., commercial batches or lots. Therefore, the test has no direct relevance for consumers or patients. The test is only conducted on test products to get regulatory approval. Commercial products are only tested using the above-mentioned invalid drug dissolution test.

Like the drug dissolution, the BE test has not been validated or authenticated, i.e., the validation for its intended purpose.

BE test monitors the release of a drug from its product in human subjects, unlike the dissolution test, which monitors the same characteristic in a round bottom beaker.

In a BE test, 18-24 subjects are administered two different (test and reference) drug products (such as tablets or capsules). Following the administration, blood samples are withdrawn from the subjects to measure the blood drug levels, which indicate drug release in the body or the GI tract. If the blood levels from both products are similar, with acceptable variability or variance, then the products are considered BE. It means both products are presumed to have the same therapeutic effect. This forms the basis of generic product development. i.e., showing a generic product (test) is equivalent to its branded (reference) version.

The question is, does this test monitors the sameness in the drug release of the test and reference products? That is, has this test been validated for this purpose? The answer is no. Such validation requires products having known and established drug release characteristics.

However, no such reference standards or products exist.

So in current practices, comparative studies are conducted with brand-name and generic products. If the drug release comes out within 80 to 120% of the branded, the generic is declared acceptable and promoted as a high-quality product with a science-based assessment.

This acceptable difference in drug release within the 80 to 120% range is an arbitrary standard. It assumes that if the difference is 20% lower or higher than the reference product, the body would not recognize such a difference and will consider the product as the same or equivalent.

The troubling part is that 80 to 120% difference is assumed to be because of the products, but in reality, it is the physiological difference in body drug absorption mechanism, i.e., bringing a drug from the GI tract to the bloodstream (link). The product has no contribution to this variability. So it means the BE testing does not assess product characteristics but the body's physiological variability. In fact, the physiological variability could be even higher depending on the subjects' or study requirements, such as testing with or without a meal. The point is that the test has higher variability than expected for the tested item. How could such a test be allowed? Medical and pharmacy-dominant experts are not aware of this flaw. It is a blatant reflection of a lack of competency or ignorance of science, particularly the science of testing or analytical chemistry. This is a fundamental principle of the analytical testing which is being violated.

So, experts and authorities are not following science in developing or assessing drug products. Hence, they are teaching or guiding the industry with false science. Therefore, the drug products one obtains cannot be claimed to have the desired and scientifically valid attributes.

As a side note, the current COVID-19 pandemic is monitored with in-house (CDC) developed tests, known as PCR or Antigen. Unfortunately, these tests are also not validated because, for validation, one requires reference standards of the virus, its RNA, or spike protein, which are missing as well. Without validation, a test cannot tell anything, hence the fakeness or fraud of the virus and its pandemic (link).

The practice of using invalid tests is ingrained in the regulatory system. It reflects the ignorance and incompetence of the science at the regulatory authorities.

One may ask how and why such a fraudulent practice has not been caught and addressed. The reason is that the system is controlled and managed by a peer-review system. No independent third-party review or audit is allowed. Opinions by third parties are considered irrelevant and/or conspiracy theories, as reflected by the censoring of often valid scientific questions and thoughts.

An urgent audit of the so-called science practices within the regulatory authorities is urgently needed. In the meantime, any claim referencing science by medical and pharmacy

professionals concerning creating medicinal products should be put on hold.

To conclude:

1. The guidance the authorities and experts provide on product development and assessment is based on false and fraudulent science.

2. An urgent audit by an independent third party, not peers, is needed to stop the fake science practice.