Editorial

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The Theranos saga and the consequences

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In this issue, *CCLM* publishes a final opinion paper on the Theranos story by Fiala and Diamandis [1]. Theranos has collapsed after allegations of an “elaborate, years-long fraud in which they exaggerated or made false statements about the company’s technology, business, and financial performance” by the Securities and Exchange Commission [2]. We do not know exactly what happened. In any case, several questions remain. The major question is probably who was harmed and could this have been prevented. The second part of the question leads to the consequences that should be derived from the Theranos case.

Let us briefly summarize the technical and medical claims of Theranos. First, the CEO Ms. Holmes claimed that Theranos developed a technology enabling the measurement of numerous analytes from a single drop of blood obtained by finger prick. Second, she claimed that the underlying technology would lead to substantially lower prices for laboratory tests. And third, she claimed that “by empowering individuals to engage in their own health, we can build a preventive care system in America”.

The first claim is a purely technological issue that could be easily verified by established standard procedures. The second issue is of interest because it would have been easy enough to find out that reimbursement for lab tests has little to do with real costs. This can be verified by comparison of reimbursement schemes in different countries. On an international level, Theranos prices were not highly competitive. The third issue is the direct-to-consumer (DTC) marketing of lab tests. The finger prick approach would have simplified this significantly, if it had worked. This was perhaps the major attraction for investors. Of the three claims made by Theranos, DTC lab tests have perhaps the broadest implications for future rules and regulations.

So, who was harmed? Apparently, investors and cooperation partners were harmed significantly. Could this have been prevented? If they had looked more closely and had involved experts in laboratory medicine, they would have probably developed doubts regarding the technology. However, history is full of people who transfer money to impostors with the expectation of huge revenues. Quite commonly, they are driven by the fear that

someone else might make the deal. Basically, Theranos is the old story of greed, fraud and credulity. Common sense and scientific doubt are the only remedies.

What about the general public and patients? So far it appears that the intervention by the authorities came late, but not too late. Perhaps, the investigation by John Carreyrou of the *Wall Street Journal* helped to speed up this process. Do we need more rigid regulations for diagnostic tests? This is a difficult issue. There are good reasons to have different levels of regulation for diagnostic tests. Both the US Food and Drug Administration (FDA) as well as the in vitro diagnostics (IVD) regulation of the European Community leave room for laboratory developed tests (LDT) under certain conditions. It is beyond the scope of this editorial to discuss this in detail. The reader is referred to the appropriate publications [3, 4] and a commentary on Theranos’ exploitation of FDA regulations [5]. Regulatory provisions permit (academic) institutions to develop and implement tests for in-house use with a reasonable amount of validation. Extensive documentation and validation of LDTs would be prohibitive for most academic institutions with the consequence that novel diagnostic tests would be developed exclusively by diagnostic industry as is the rule in drug development. Thus, with any regulation, there are two sides of the coin. However, we should keep in mind that different from Theranos, most academic institutions do not hesitate to make their efforts public and have them reviewed by their peers. This was definitely not the case with Theranos, and secrecy was the major criticism raised in early comments on Theranos long before the whole problem surfaced [6, 7].

However, in our opinion, there remains one major issue, which was also mentioned in several articles dealing with Theranos, i.e. DTC. Current regulations are based on the concept that laboratory tests are ordered and interpreted by physicians not by lay people. In theory, this ensures an equal information level between the parties. On the other hand, asymmetric information which is a common cause of market failure, is inherent to the direct laboratory-patient relation. Therefore, there is an increased need for protection of laypersons, if diagnostic tests shall be marketed to the public [8]. To elucidate this issue, we would like to draw attention to an article which appeared in *CCLM* 3 years ago. In this

article, Johnson and coworkers [9] tested the performance of pregnancy tests. One irritating finding was that several tests did not reach the sensitivity claimed by the manufacturers. Some tests were even marketed with the claim to detect pregnancies already 8 days after conception, which would be a diagnostic challenge considering the distribution of urinary human chorionic gonadotropin at this point in time. The study was initiated by the authors who are all employees of a manufacturer of pregnancy tests and may therefore be biased. No regulatory authority was involved. However, it illustrates that laypersons are most likely unable to validate technical or medical claims of diagnostic tests.

Thus, we would like to make a plea for more stringent regulation of laboratory tests or services, which are intended to be marketed directly to the lay public. Commercial providers of DTC diagnostic tests should be required to substantiate all analytical and medical claims by relevant data before market access. Although regulation of analytical performance should be relatively straightforward, medical claims will be a major challenge. The ongoing debate regarding the pros and cons and the timing of PSA screening is a good example of the difficulties that will be encountered here [10]. This implies that DTC might require long-standing experience with the diagnostic value of a test under traditional conditions.

CCLM decided to publish the series of articles on the Theranos saga to contribute to an open discussion on future developments deeply affecting laboratory medicine. For all innovative IVD methods and systems, accurate validation is needed to ensure the essential role of laboratory information and its increasing importance for patient safety. Laboratory services may provide the foundation for a safe, effective and equitable health care delivery not only assuring accurate analytical quality but covering the entire steps of the process starting from appropriate request and ending with accurate interpretation/utilization of laboratory information. When the general public shall be enabled to order tests, it must be ensured that people are informed properly to be able to order appropriate tests and interpret them correctly. Whether some sort of “diagnostic stewardship” can be implemented for the public awaits proof of principle [11]. In any case, the Theranos experience should sensitize us for the inherent risks and fuel the ongoing debate on this topic. Peer-reviewed journals can provide an appropriate forum for this debate. We are working for a future without “predatory” journals [12] and predatory IVD companies.

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