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TranspariMED's comments on the FDA Draft Guidance "Civil Money Penalties..."

The following are TranspariMED's comments on the FDA Draft Guidance "Civil Money Penalties Relating to the ClinicalTrials.gov Data Bank," as published in September 2018.

TranspariMED is an initiative that works to end evidence distortion in medicine, with a particular focus on clinical trials. It is based in Bristol, UK, and works globally.

SUMMARY

TranspariMED urges the FDA to issue a new Draft Guidance that fully aligns the work of FDA with the letter and spirit of FDAAA, Congressional intent, and the FDA's own mission. In particular, in order to strengthen compliance with FDAAA and its Final Rule, the FDA should:

- **Comprehensively monitor compliance**
- **Routinely impose fines for all violations of the FDAAA reporting requirement**
- **Immediately initiate three simple steps to strengthen compliance through 'nudging'**

BACKGROUND

TranspariMED welcomes that the FDA finally seems to be moving towards enforcing the clinical trial registration and reporting provisions of the 2007 Food and Drug Administration Amendments Act (FDAAA) and its Final Rule.

However, the current Draft Guidance falls significantly short of bringing the FDA into compliance with the provisions of FDAAA (in particular 42 CFR part 11) and its Final Rule.

The current Draft Guidance also falls significantly short of aligning the FDA's monitoring and enforcement activities related to FDAAA with the FDA's own mission of "ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices... and by helping the public get the accurate, science-based information they need".

TranspariMED's detailed comments on the Draft Guidance are below.

MONITORING OF COMPLIANCE

FDAAA clearly mandates that FDA monitor responsible parties' compliance with the law. In contrast, the Draft Guidance suggests that the FDA only intends to monitor compliance selectively. This runs directly counter to the letter and the spirit of FDAAA, and the mandate and direction provided by Congress.

Unreported clinical trials undermine the evidence base on drug safety and efficacy. Past experience strongly suggests that compliance monitoring and publication of monitoring data is a strong driver of responsible parties' compliance with clinical trial reporting requirements. Therefore, the FDA should systematically and comprehensively monitor compliance with FDAAA registration and reporting requirements, covering every trial subject to these requirements, and routinely publish line-by-line monitoring data.

This should include monitoring whether data entered into Clinicaltrials.gov by responsible parties is complete, accurate, and kept up to date. In this context, the FDA should take note of the recently revised WHO International Standards for Clinical Trial Registries.

ENFORCEMENT OF COMPLIANCE

FDAAA provides the FDA with the mandate to impose fines on responsible parties that violate the requirement to post trial results on Clinicaltrials.gov. However, the FDA has so far failed to issue a single fine despite widespread and well-documented violations of this key FDAAA requirement. According to data aggregated by the "FDAAA Trials Tracker," over one billion U.S. dollars (\$1bn) in potential fines have remained uncollected by the FDA since the Final Rule came into force in early 2018. This runs directly counter to the letter and the spirit of FDAAA, and Congressional intent.

The FDA should ensure that notices of noncompliance are rapidly and routinely issued to the responsible parties for each and every clinical trial that is in violation of the FDAAA reporting requirement. The FDA should further make all notices of noncompliance publicly available on ClinicalTrials.gov.

The FDA should issue a new Draft Guidance that makes the imposition of fines for violations of the FDAAA reporting requirement a routine part of the FDA's work, in order to drive improvements in compliance as per Congressional intent. Note that this would directly and substantially benefit the U.S. Treasury. In addition, by strengthening the medical evidence base, it would benefit U.S. patients.

STRENGTHENING COMPLIANCE THROUGH 'NUDGING'

The current Draft Guidance omits to mention three simple steps the FDA could take to substantially improve compliance with FDAAA reporting requirements. The FDA should initiate these steps immediately, as doing so requires no formal Guidance.

- First, the FDA should via email contact the responsible parties of all clinical trials subject to the FDAAA reporting requirement that have not reported results to remind them of the reporting requirement.
- Second, the FDA should routinely via email remind each responsible party of the reporting requirement on several occasions before the trial results become due.

- Third, when a new trial subject to FDAAA reporting requirements is first being registered, the Clinicaltrials.gov interface should require the responsible party to 'agree' to comply with the reporting requirement (e.g. by ticking a box) before the trial registration process can be concluded.

The literature on behavioural economics and 'nudging' strongly suggests that each of these three steps could substantially improve compliance rates at negligible cost, in particular among smaller trial sponsors, and especially if the FDA uses experimental approaches to determine which messages are most effective.

TranspariMED hopes that the FDA will issue a new Draft Guidance incorporating the elements discussed above as rapidly as possible.

With best wishes,

/s/

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