Some Major FDA EUA/Approval Reforms Needed

1 - Based on what transpired with COVID-19, the FDA needs higher standards before giving an Emergency Use Authorization (EUA) **or** an official **Approval** for:

a) A vaccine (***particularly when a reasonable therapeutic is available***).

b) A therapeutic (*e.g., remdesivir and molnupiravir should not have received EUAs*).

2 - Some key elements of the higher standards that the FDA needs to adopt (for giving an EUA or an Approval, for a vaccine or a therapeutic):

a) A requirement that RCT control groups must be given reasonable medical care (not zero treatment), as that is unethical and results in unscientific test results.

b) A requirement that all RCTs (and subsequently the FDA) publicize *Absolute Risk* — preferably, exclusively.

Note 1: This is consistent with an important FDA advisory publication. A key conclusion (*see page 60*) is that the public is: "unduly influenced when risk information is presented using a relative risk approach; this can result in suboptimal decisions. **Thus, an absolute risk format should be used**."

Note 2: The CONSORT 2010 Statement — Updated Guidelines for Reporting Parallel Group Randomized Trials states: "… **presentation of both absolute and relative effect sizes is recommended**…"

b) A requirement that the **absolute** effectiveness (not **relative** effectiveness) conclusively demonstrate that the vaccine or therapeutic is a net societal benefit.

c) A **minimum effectiveness** should also be required (e.g., 50%) to be granted an EUA.

d) If after an EUA is granted, subsequent scientific studies indicate that the efficacy rate appears to have gone below the minimum efficacy, then the FDA should promptly have a formal public hearing of their EUA. If the conclusion of the public hearing is that there is a reasonable likelihood that the efficacy now appears to be below the minimum required, the FDA should immediately revoke its EUA.

e) The FDA's *Fact Sheet for Healthcare Providers* include a warning statement like: "This EUA was granted after a very limited scientific assessment of this product for this medical condition. As a result, the FDA has a **low confidence level** regarding the **efficacy** or **long-term safety** of this product for this condition."

f) The FDA's *Fact Sheet for Healthcare Providers* include a warning statement that this is an experimental EUA product, so it is **not** appropriate for it to be mandated.

g) The FDA should prohibit any EUA recipient from advertising that their product is "safe and effective," as neither has been scientifically adequately determined.

h) The FDA must be prohibited from granting an EUA based on a subset of any RCT results (e.g., like here).

3 - Considering that the majority of adults in the US have at least one chronic disease, the FDA needs to meaningfully address this reality (when giving an EUA or an Approval, for a vaccine or a therapeutic) by the following:

- **a)** A requirement that RCTs must include a representative sample of chronic illness subjects in both testing and placebo groups for products seeking EUA or Approvals.
- **b)** In ALL cases where "a" was **not** done, the FDA's *Fact Sheet for Healthcare Providers* must specifically include a warning statement (*necessary for informed consent*) that testing was **inadequately done** on subjects who had a wide variety of other chronic ailments, so the consequences to recipients with those conditions is unknown, and may **worsen** (including **death**) when taking this EUA product.

4 - The FDA should be obligated to promptly develop and publicize regulations for *Informed Consent* regarding the public's taking of EUAs. (These should be comparable to the FDA's informed consent conditions for clinical trial subjects [which includes many pages of conditions and caveats: see here].) **EUA product recipients should effectively be considered to be clinical trial subjects**

5 - Regarding off-label use (again in an emergency), the FDA should:

- **a)** Make it allowable for medical practitioners to prescribe an off-label therapeutic for any condition, when the medical practitioner believes that there is reasonable scientific evidence of efficacy. (Note: *The FDA's website states that this is already the case, but the COVID-19 situation — e.g., with IVM and HCQ — indicates otherwise.*)
- **b)** Be prohibited from identifying an off-label therapeutic as **not acceptable** for a medical practitioner to prescribe for a condition, where the medical practitioner determines that there is reasonable scientific evidence of safety and effectiveness. (*This prior misleading FDA webpage convolutes self-medicating and/or humans using veterinary products [never advisable], with a medical practitioner prescribing IVM.*)
- **c)** Establish an alternative procedure to an EUA for repurposed (esp. non-patented) pharmaceuticals, where they temporarily receive the FDA's blessing, while more comprehensive scientific testing is conducted. Not doing this would appear to be contrary to this statutory directive.
- **d)** Have sizable funds specifically allocated and available to quickly pay for independent RCT testing of off-label options that have reasonable scientific evidence of their effectiveness and safety for a repurposed medical use. (See 21 USC Chapter 9, Subchapter V: §355g. Utilizing real-world evidence.)
- **e)** Have a Consumer Advocate who does nothing but promote non-patented, re-purposed drugs to the FDA for review (especially in an emergency).

john droz physicist North Carolina 1-15-25