Background Q&A for the Mandatory Alternatives Petition

Q: Who is the MAP coalition, and why is it interested in drug testing on animals?

The MAP coalition is a network of organizations that advocate for replacement of animal drug testing methods that are inaccurate, unvalidated, immensely cruel, and often dangerous for human health. The coalition members are concerned at the number of hazardous drugs approved for human use, the harm they're causing millions of people around the world, and the inability of animal testing methods to detect and prevent these serious consequences.

[More reliable testing methods are available, and many more are in development, which can produce safer and more effective drugs than current animal testing methods. Due to the failure of the FDA to adopt and implement such alternative methods in a timely and effective manner, the member organizations of the MAP coalition have come together to petition the FDA to mandate the use of scientifically sound alternatives to the use of animals.]

Q: What are the reasons for the MAP?

Our coalition of organizations has prepared this petition to the FDA because there has been little progress in the adoption of scientifically sound replacements for cruel and unreliable animal tests.

[Despite the availability of numerous suitable alternative products, and the establishment of the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) a decade ago, animal testing is still in most instances the default expectation by the FDA and companies. Neither the FDA nor the companies it regulates have demonstrated significant progress toward developing or adopting human-specific methods to improve drug testing accuracy and replace cruel animal testing. This inertia has contributed not only to the very high failure rate of drugs in clinical testing, but to the approval of dangerous drugs and the occurrence of more than 100,000 deaths annually in the U.S. from adverse drug reactions.]

Q: What are we asking the FDA to do?

The FDA could be doing much more within its current authority to replace animal tests with superior non-animal methods. We are asking the FDA to assert leadership in advancing drug testing from archaic and unreliable animal methods to scientifically sound and humane methods.

[We have recommended several approaches that would be beneficial, including: (a) stronger industry guidances to discourage submission of unnecessary animal test results; (b) standardization of FDA reviewer practices so animal tests are not requested when not required; (c) harmonization of implementation practices with the EU and Japan; (d) development of a FDA policy for the designation and adoption of “scientifically satisfactory” replacement methods; (e) making maximum use of the extensive FDA human drug database to eliminate the perceived need for much animal testing; (f) adoption of more of the available non-animal methods, and; (g) mandatory implementation by companies regulated by the FDA.]

Q: How does the U.S. compare with Europe in the area of alternatives adoption?

The European Union is well ahead of the U.S. and the FDA in identifying and adopting testing methods that replace or reduce animal use in drug development and testing.

[The linchpins of this advantage for Europe are the 1986 EU Directive 86/609/EEC mandating the use of non-animal methods when they are available and approved, and the proactive efforts of the European Centre for the Validation of Alternative Methods (ECVAM) to make scientifically sound methods available. There is no such legislation in the U.S., the FDA is passive in this regard, and ICCVAM has impeded rather than promoted adoption of new methods.]

Q: Why are animal tests the standard practice for drug testing?

In response to the thalidomide disaster in the early 1960s, congress and the FDA decided that all new drugs should be tested for safety in animal studies before being approved for human testing. It was assumed that animals would respond to drug tests like "little humans," but the ensuing decades have shown that the opposite is true – animals respond differently and unpredictably.

[The paradigm of animal testing has never been validated for safety or efficacy prediction, but the FDA "is comfortable with it," and hasn't been proactive in seeking better methods. Conversely, newer methods must navigate onerous validation hurdles, which to date have led to the rejection of a very high percentage of methods presented to ICCVAM.]

Q: How accurate are the animal test results the FDA receives?

The statistics show irrefutably that methods used in preclinical testing (mostly animal methods) to select drugs for human testing and later human use are unreliable. This is acknowledged by the FDA, by the Health and Human Services Department, and by the pharmaceutical industry.

[After all the preclinical testing, including the animal tests, the FDA reports that 92% of drugs approved for testing in humans fail to receive approval for human use. This failure rate has increased from 86% in 1985, despite all the advances and refinements intended to make animal tests more accurate. The failure rate is at least 95% for cancer drugs.

More than half of the few drugs approved are withdrawn or relabeled due to serious or lethal adverse effects, and there are more than 100,000 deaths from adverse drug reactions annually in the U.S. This is the equivalent of the crash of a full Boeing 777 plane every day of the year.

It takes approximately 100 new drug candidates tested in humans to produce just one safe and effective drug that is not a "me-too" drug. And according to pharmaceutical company experts, as many as 90% of these approved drugs will only work in 25-50% of patients. It is hard to imagine a more failed paradigm for drug testing.]

Q: What are the consequences of these unreliable animal tests?

Animal drug tests are largely unable to detect dangerous drugs before they are given to people.

[In addition to the startling adverse drug reaction statistics above, there have been dozens of lethal drugs approved for human use after demonstrating safety and efficacy in animal studies. Some of the better known examples are Vioxx, hormone replacement therapies, Rezulin, Baycol, Butazolidin, phenformin, Seldane, and DES. Vioxx was the worst drug disaster in history, causing an estimated 60,000 deaths in the U.S. alone (more Americans than died in the Vietnam War) and more than twice that many deaths worldwide.]

Other drugs successful in animal studies have been total treatment failures when given to people.

[Examples include **all** of more than 80 HIV/AIDS vaccines, **all** of more than 150 stroke treatments, **all** of more than two dozen drugs that cured diabetes in mice, and **all** of more than two dozen treatments for spinal cord injury.]

Animal tests also produce false adverse results for drugs that are safe and useful for people.

[Examples include aspirin (birth defects in seven animal species tested, but not in women), penicillin (kills guinea pigs and hamsters), acetaminophen (kills cats), and many others.]

Q: What are some examples of good alternatives to current animal drug tests?

The Multicentre Evaluation of *In Vitro* Cytotoxicity (MEIC) is a well-validated in vitro screening method proven to predict acute toxicity in humans more accurately that animal tests.

The U.S. National Cancer Institute employs human tissue and cell methods in three areas it found animal tests to be poor predictors: (a) The DTP Human Tumor Cell Line is used to screen compounds for anti-cancer effects; (b) The DTP AIDS antiviral screen uses human HIV-1 cell lines to identify compounds with anti-HIV activity; (c) A panel of about 100 human cell lines is used to screen compounds for cytotoxicity (cell damage).

More than 20 replacement and reduction alternatives have been validated by ECVAM. Several human tissue models have been proven superior to the Draize eye and skin tests. Microdosing has been proven to describe drug metabolism in humans better than animal tests. Microfluidics methods such as the "human-on-a-chip" have proven to be accurate and are being improved rapidly. Human patient-drug databases and "virtual clinical trials" can replace many animal tests.