



**CBRA White Paper
Genetically Modified Organisms and Biomedical Research**

CBRA Statement

While many in the public sector consider genetically modified organisms (GMOs) to be an agriculture/biotechnology issue, genetic modification and genetic engineering also play a significant role in providing life-saving therapies, and ongoing biomedical research. Currently in California, many counties and municipalities are considering banning GMOs. Largely targeted at agriculture and crops, the wording of many of the proposed bans could/would have unforeseen and unfortunate consequences for biomedical research. For example, Measure B that passed in Marin County in November 2004 defined GMO as "...an organism, or the offspring of an organism (exclusive of human beings and fetuses), the DNA of which has been altered or amended through genetic engineering. Genetic engineering is defined as alternation or amending DNA using recombinant DNA technology, and excludes traditional selective breeding, conjugation, fermentation, hybridization, in vitro fertilization, un-directed mutagenesis, or tissue culture." Fortunately, an exemption to Marin County's Measure B excluded medical research from this ban, thereby allowing the continuation of life-saving research and treatment possible within the county. Measure M proposed in Humboldt County stated, "Section 1. Finding. The people of Humboldt County wish to protect the county's agriculture, environment, economy, and private property from genetic pollution by genetically modified organisms. Section 2. Prohibition. It shall be unlawful for any person, firm, or corporation to propagate, cultivate, raise, or grow genetically modified organisms in Humboldt County." No exemption for medical research or pharmaceutical development was offered. Though this measure was defeated, it demonstrates the tendency toward regulation of GMOs without consideration of the serious consequences to medical research.

Such bans on GMOs within counties in California, especially without medical research exemptions, could outlaw many new and critical forms of biomedical research, and adversely affect human and animal health by prohibiting many areas of research ranging from the use of transgenic animals in research such as mice and fish (they would be illegal), to genetically modified bacteria, to genetically modified plants that are used to create antibodies and produce vaccines. In addition, such bans would also prohibit the production of GMOs for research purposes, and the development and production of treatments and cures derived from GMO materials.

GMOS in Biomedical Research

A GMO is an animal, plant, or microorganism that has genes that have been modified using the gene technologies of molecular biology. This is a process where the traits or characteristics of an organism are changed by modifying genes within a species or transferring individual genes from one species to another (transgenics). The modification of genes can occur by: eliminating certain genes altogether within an organism, modifying genes by turning them off or on, or altering their location, or adding copies of specific genes from other organisms. Other associated terminology includes genetic engineering, and transgenics or recombinant DNA (inserting a gene from one species to another).

The use of genetically modified organisms represents an *enormous* advance in the science of biological and medical research, and GMOs are playing an *increasingly* important role in the discovery and development of new medicines. Most diseases, from cancer to dementia, are partly caused by our genetic makeup and over 10,000 diseases are caused by a single faulty gene. GMOs can help researchers to understand the workings of human *and* animal genes, and allow researchers and scientists to better understand the role of genes in specific diseases.

GMO-based medical research is also fundamental to developing new ways to treat and cure: to create and produce vaccines to prevent disease (for example a vaccine for HIV), to develop new and more efficient ways to create antibodies for the treatment of disease, and to develop and manufacture pharmaceuticals. For example, until the mid-1980's most insulin was produced by extracting a human-equivalent insulin from the pancreas of animals (usually pigs). Thanks to GMO-based research, the genetic sequence for insulin was removed from human DNA, and then inserted into the DNA of a bacteria (*Escherichia coli* -E. coli). Insulin for treating diabetes has now been produced with this genetically engineered bacteria for more than 20 years (Sales for this insulin, Humulin were more than \$1 billion in 2003). Likewise, genetic modification in bacteria has resulted in the production and marketing of human growth hormone and somatostatin, and a genetically engineered version of erythropoietin, a protein that simulates the formation of red blood cells had more than \$2.4 billion in sales in 2003. Clearly, genetically engineered medicines are in great demand.

In addition to protein drugs, research on antibodies and vaccines developed through recombinant DNA and genetic modification is an emerging market. While there are not currently a large number of vaccines so derived on the market and in use at the clinical setting (both human and veterinary care), research underway shows amazing promise and vaccines and treatments using these techniques will soon be very common and widespread. For example, a new vaccine based on genetically modified peanut proteins could protect people with peanut allergies from developing a life-threatening allergic response, and researchers are working on genetically engineering bacteria to prevent cavities and tooth decay.

Because isolating antibodies in large quantities is difficult, genetic engineering offers great promise for not only developing treatments and cures using these methods, but also in making such treatments widely available and affordable. GMO production methods in bacteria and plants have the potential to lower the time and cost for vaccine production, while at the same time offering a wide range of advantages. Often called “biopharming” genetic modification within a plant allows for researchers to more rapidly develop organisms that exhibit certain characteristics, produce needed biologicals, or offer genetic models necessary for medical research and the development of treatment, vaccines, or cures. In addition, the treatment for numerous human (and animal) ailments such as cancer, herpes, and infectious diseases require human and viral proteins (antibodies, enzymes, etc.) that can only be derived from living systems. Currently, the majority of these drugs are based on such material taken and cultivated from animal cell cultures. However, the production of such needed antibodies from animal cells is expensive, making the resulting drugs too expensive for most patients. Second, and more critical, there are simply not enough of these materials being produced to meet existing demand, much less projected future demands based on the number of new drugs in development. When reviewing the therapies currently in development, by 2010 there could be more than 30 antibody-dependent products competing for this same basic supply of materials.

Many genetically modified plants have already proven critical information and are in use to produce such necessary antibodies, and continue to offer great promise. Pond algae, tobacco plants, and soy are only a few of the many plants that have contributed greatly to medical advancement. Exploration and continued development of GMO-based protein expression is necessary if we are to produce affordable, life-saving medicines for the future. There are no current means to express such proteins outside of living cells.

GMOs and Transgenic Animals

While most often regarded as a crop or plant issue, “Genetically modified organisms” or GMOs also includes genetically modified animals that are frequently a part of biomedical research. Like other forms of genetic modification, animals can be genetically modified in several ways, for example by removing genes from its DNA structure or by adding new. Gene knockouts allow researchers to delete individual genes from animals, giving us valuable clues as to what those genes do. In others modifications, researchers introduce new genetic material into suitable hosts (typically rodents), from other species, often human. Commonly referred to as transgenic, these animals have been genetically engineered/modified to create new or isolate existing characteristics. In many cases this has no noticeable effect, while in some cases the alteration leads the animal to develop the equivalent of a human disease being studied.

These transgenic animals have proven to be an important way to not only study a disease, but also to treat or even cure a disease. As an example, to get specific human antibodies for use in drug development, mice have been

developed that are capable of making fully human antibodies, in place of the normal mouse antibodies that are normally generated. Such mice can be injected with cells or material from a human tumor or an infectious agent. The mice respond with a human antibody response instead of a mouse antibody response. Researchers then immortalize the antibody-producing cells from the mice into special nutrients so they multiply, producing therapeutic quantities of monoclonal antibodies. As a result of such research, at least 33 fully human antibodies have been tested in human clinical trials to date. These antibodies are analogous to approved antibody therapeutics such as Erbitux for colorectal cancer; Remicade and Humira for rheumatoid arthritis; three drugs for preventing organ transplant rejection and Xolair for asthma. While almost all of the aforementioned antibodies are originally mouse in origin, the transgenic mice that produce fully human antibodies are a potential advantage over these therapeutics as their antibodies are fully tolerated in humans; mouse-derived antibodies can be quickly rejected. None of these advances would have been possible without research using genetically modified organisms.

Other examples of GMOs or transgenic animals being used in medical research include transgenic goats to produce TPA or tissue plasminogen activator, and Antithrombin 3 for the treatment of blood clots; Factor 8 and factor 9 being produced in sheep for the treatment of blood clotting disorders such as hemophilia; and human protein C in pigs for use as an anticoagulant; the development of CFTR for the treatment of cystic fibrosis; and the production of MSP-1 antigen in transgenic mice. MSP-1 produces a human antibody response to malaria, and could be the basis for an eventual malaria vaccine. Researchers are developing techniques for gastrointestinal disturbances, rheumatoid arthritis, Alzheimer's Disease, and cures and vaccines for hepatitis and herpes infections. Researchers are working with dairy cattle to produce milk with an inactive b-lactoglobulin milk protein so that people with lactose-intolerance can eat dairy products. Another role genetically modified or transgenic animals play in research is xenotransplantation – the production of tissues and organs in animals for human use. New heart valves from pigs are an important example.

Pharmaceutical products derived from genetically modified organisms are also developed for veterinary use. An example is the use of a recombinant vaccine-rabies virus for vaccinating foxes against rabies, which is more efficacious and safer than the conventional attenuated SAD B19 strain. This strain, which is still used sometimes, is pathogenic for some non-target mammals. Another is the recombinant Merial canarypox DNA vaccine (for West Nile Disease) that incorporates WNV membrane and envelope proteins into the canarypox DNA and expresses these proteins following administration. Research is also currently underway using forms of GMOs to address Bovine Spongiform Encephalopathy (BSE - mad-cow), various influenzas, feline HIV and leukemia, among many others.

Concerns Regarding GMOs

One of the most common fears about GMOS in the plant world is the possibility of plant-based GMOs mixing with food supplies, or the potential of transgenic animals breeding with native population. To prevent this, biomedical researchers have turned to producing the pharmaceutical products in non-food, or feed crops such as tobacco (*Nicotiana tabacum*), duckweed, and others to produce a wide range of human proteins to treat illness, including anticoagulants, growth hormone, Hepatitis C and B treatments, human interferon, liver cirrhosis, human serum, and cystic fibrosis. Regulation of transgenic organisms, including genetically modified or transgenic plants, is shared by three agencies: the Environmental Protection Agency, the Food and Drug Administration, and the USDA – and at the local level, the California Department of Fish and Game oversees transgenic aquatic species. Research facilities are secure, research animals carefully housed and cared for, and no transgenic animal is allowed to breed with wild populations.

In addition, the United Nations, World Health Organization, American Medical Association, and the National Academy of Sciences have examined the health and safety issues of GMOs. The UN recently reported that genetically modified crops "pose no more risk than conventionally grown crops" and "there have been no verifiable reports of their causing any significant health or environmental harm."

There are also concerns about the use of transgenic animals in research. In particular that these animals suffer more abnormalities, are more likely to be destroyed and that they could have a negative impact on wild populations if they are accidentally released. All animal-based research is subject to rigorous government regulation and inspection.

In addition to profoundly benefiting biomedical research and by association offering dramatic developments in medical treatment and improvements in human and animal health, using genetically modified animals can be good for animal welfare because: Fewer animals can be used for each experiment because researchers get more accurate results; the use of transgenic mice is helping to reduce the number of other animals needed for medical research. For example one pharmaceutical company has helped develop a new safety test for the polio vaccine that uses transgenic mice, rather than monkeys; researchers can use simpler animals like fruit flies and earthworms, or rats and mice instead of using complex animals like primates; and in many cases, researchers don't even need to take blood samples from animals to test for proteins because they can get them to produce those proteins in their milk.

Benefits of Biomedical Research

Nearly every major medical advance of the last 100 years has depended largely on research with animals. We have made significant progress against diseases such as polio, small pox, cancer, heart diseases, and diabetes among many, thanks to animals. Our best hope for developing preventions, treatments, and cures for diseases such as Alzheimer's, AIDS, diabetes, cancer, and treating human and animal conditions will involve biomedical research on a wide spectrum of genetically modified plants, animals, and bacteria.

The impact that GMOs have made, whether speaking of GM bacteria or GM cows, is immeasurable, saving lives and improving animal *and* human health *today*.

Wide-sweeping legislation, intended for agricultural crops, is predicated on fear and inaccurate claims, and threatens to ban the presence and use of *all* GMOs. Such a widespread ban essentially puts significant medical advances at risk, is detrimental to the discovery of new therapies, treatments, and cures, and threatens to reverse progress made over the last several decades.

Banning GMOs will impact critical biomedical research, could potentially affect the significant role transgenic animals and plants play in biomedical research, and curtail the discovery of much-needed therapeutic antibodies, vaccines, care, treatment, and cure.

While regulations and strict guidelines must be a part of any GMO undertaking, bans on the technology are tantamount to stepping backward in time and rejecting the life-saving advances that technology has provided.

TO SUPPORT THE ADVANCEMENT OF HUMAN AND ANIMAL HEALTH BY PROMOTING AND PROTECTING BIOMEDICAL RESEARCH AND TEACHING.