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Review Article

Considering Ethics in Agricultural Experimental Research with Special Mention to Agricultural Biotechnology Research

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ABSTRACT

Ethics in experimental research equals scientific integrity, a notion principle particularly stressing honesty while implementing discipline concepts on what is excellent and terrible. Some moral responsibility is defined through specifically agreed standards in doing experimental research. Ethics of experimental research in agriculture involves all activities done before, during, and after the study, consisting of personal, research, and social ethics. Ethical code and policy include, but are not limited to, honesty, objectivity, integrity, carefulness, openness, intellectual right recognition, confidentiality, responsible publication, social responsibility, competency, legality, and protecting research object/subject (plant, animal, human) from possible unfair manipulation. One development triggering the controversy of agriculture's experimental ethics is the progress of agricultural biotechnology which resulted in genetic engineering products. Rules, regulations, and laws concerning the use and development of genetic engineering in agriculture to avoid adverse effects of these products, such as rising environmental hazards, increasing human health degradation, and unfair economic competition, should be considered and implemented.

Keywords: agricultural biotechnology; ethics; experimental research

INTRODUCTION

Ethics may be defined as a behavior, norm, or perspective that differentiates bad and good conditions acceptable to a certain and definite social group. Meanwhile, bioethics is an ethics study in the discipline of biology and medicine. In agricultural study, a branch of biology (i.e. applied biology), ethics is viewed as the wider application of bioethics, including ethics assessment toward all actions which may help or disturb an organism (Fossey, 2007). Ethics is a kind of scientific integrity, a thinking principle based on honesty, applying conceptual discipline in judging what is bad or good as a moral obligation through determined behavioral rules and standards. In the philosophical context, ethics becomes a reflection of communal morality, so that ethics may also be called moral philosophy (Feynman, 1974).

Experimental research is research that tries to explore and discover the effect of certain variables toward other variables in controlled conditions, where the independent variables are manipulated by the researcher (Tyasning, 2011). Arikunto (2006) states that the experimental research method is a technique to find a causality relationship between two factors deliberately chosen by the researcher by eliminating, suppressing, or canceling troublesome factors. In agricultural disciplines, for instance, experimental research may be found in the discipline's branches, such as planting culture, plant's pests and diseases, agricultural technology, and agricultural socio-economics.

Ethics in experimental research includes all activities before, during, and after the research (Blakstad, 2008). The pre-activities consist of planning and designing the experiment. The activities during the research

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consist of all carried out research work, including the use of organisms, up to data collecting and their analysis. Ethics after the research deals not only with writing and publishing but also with bio-security, health and environmental welfare as well. McLaren (2007) writes that ethics in biological research has three different categories: personal, research, and social ones. Personal ethics describe personal morality, including openness and responsibility; research ethics is the ethics that guide the workline of the research itself; while social ethics is the social effects that will arise from the execution of the research.

Science and research in agriculture so far have developed enormously. The development is expected to provide solutions to many problems faced by the agricultural sector. One of these developments is the progress of agricultural biotechnology, which results in genetically engineered agricultural products. These products were engineered to counter problems such as nutrition deficiencies, low crops' yield and production, and low resistance to environmental stresses (von Braun, 2010; Amin *et al*., 2011; Bryant & Hughes, 2017). In return, the developed agricultural products of genetic engineering and biotechnological manufacturing created social, economic, environmental, health, political, legal, and ethical issues concerning the products themselves. The risk that comes out of the engineered products worries society and becomes controversial. A study on the rules and regulations is definitely needed as general guidelines on how to conduct agricultural research. This article tries to disclose the ethical aspects of further experimental research in agriculture.

ETHICAL ASPECTS IN AGRICULTURAL EXPERIMENTAL RESEARCH

As mentioned above, ethical aspects in experimental research ought to be applied before, during, and after the research (Blakstad, 2008; Costello *et al*., 2016). McLaren (2007) described those three distinctive categories of biological research ethics and points out that personal ethics cover personal characters such as high morality, honesty, free of misconduct, and full of responsibility. Research ethics also includes waives for the objects one uses in organism-related research. Social ethics should be considered since the social consequences of the research may turn out to be unacceptable.

Before carrying out any research, the planning and design should be carefully outlined. The hypothesis needs to be accurately constructed, with proper relevance and limiting the biases which might have happened. The theory should be carefully examined to ensure whether it had been constructed by other researchers before. Factors pertaining to intellectual property must also be considered. Intellectual property rights will include the research results and the hypothesis itself, the underlying theory, and the research methods (Gupta, 2004; George, 2016).

Ethics in utilizing organisms (plants, animals, humans, and microorganisms) needs special attention in agricultural research. During research execution, the ethics should be correlated to research methodology, data collection, and data analysis (Burkhardt *et al*., 2005). Data collecting should be done with high accuracy and close monitoring to ensure that the collecting was done with care and honesty. Examples of questionable data analysis are: neglecting biases/non-random errors; inaccurate or simply wrongful statistical procedures; negative conclusion due to incorrect statistical calculations; or practices such as falsifying, cutting, or "delineating" data (Baumans, 2004; Punia, 2006; McLaren, 2007; Ridwan, 2013).

After the research work ends, ethics will cover issues in writing, reporting, and publishing research results. In writing, it is only proper to appreciate all contributors of the research accordingly. The authors are the main intellectual contributors of the research; therefore they are the ones who are directly responsible for the content of the report or publication, and all these contributors should be able to explain the how and why of the research. Conflict of interests and commitments usually arise from differences in professional requirements, personal needs, and financial matters. This should be resolved before finishing the research (Grimm, 2008).

The code and policy of ethics in conducting research include the following (Resnik, 2015): honesty, objectivity, integrity, vigilance, openness, honoring intellectual property, confidentiality, responsible publication, mentoring responsibility, social responsibility, competency, legality, and protection in utilizing living organisms (plant, animal, human) as the object/subject of the research. Honesty must be exercised in all aspects, both in conducting the research and communicating its results—frankness in reporting data, methods, and publication status. Objectivity should be used to avoid biases in experimental designs, data analysis, data interpretation, peer-reviewing, and others. Integrity consists of acting righteously, keeping promises, and striving to think and act judiciously. Vigilance means meticulous works to keep away carelessness and inappropriate practices: there should be good recording habits on all steps taken, from data collecting to correspondences about scientific research publications.

Openness is needed to share data, ideas, results, instrumentations, and other resources; moreover, the researcher must also be open to critics or newer and out-of-the-box ideas. Honoring intellectual property may include honoring its patent, creative process, and other intellectual rights, such as not using any unpublished data (even though one can and has access to them) and developed methods or any results without permission. Give credit and acknowledgement on anything where they are due to the right institutions or personages. Confidentiality is needed to protect any personal or covert communication, record or notes, and any unique conditions of objects/subjects of the research. Publication must be written with full responsibility and recognition of scientific advancement, not only for personal and individual gain (Allmark *et al.*, 2009). Mentoring responsibility means the researchers are ready to educate, teach and guide other researchers. Social responsibility to encourage the social promotion and reduce social hazards may be developed through research extension, public education, and advocacy. Professional competencies should always be maintained and improved, as well as legality in operating under the existing law and adhering to government policies and regulations (Blakstad, 2008; Grimm, 2008; Resnik, 2015).

Protection to any organisms used in research might be excised by avoiding unnecessary trials using organisms or not carrying out organisms-involved experiments with bad design. When the trial involves human beings, the loss and risk should be minimal while the benefit maximal. Ethical issues in agricultural research should consider the fact that agricultural sciences are applied sciences closely related to social and ecological systems. Thus, ethics in agriculture may be interpreted as the systemic thoughts on values and norms related to agricultural systems, resources management, food processing, distribution, marketing, and consumption (Shelley-Egan *et al.*, 2015).

ETHICS IN USING EXPERIMENTAL ANIMAL

Experimental animals are each and every animal used in biological research chosen under certain basic requirements or standards needed in this research (Smith & Mangkoewidjojo, 1988; Ridwan, 2013). Experimental animal management starts with selecting the right kind of animals, then prepares the care and maintenance of the animals, collects the necessary data, and usually ends by terminating the experimental animal. Rustiawan and Vanda (1990) justified the need of using experimental animals in research, i.e. (1) to minimize research subject variability; (2) to be more convenient in controlling research variables; (3) to select a shorter life cycle so multigeneration research might be conducted; (4) to select the most sensitive animal subject more easily; (5) to lower the cost; (6) to apply them to high-risk research works; (7) to obtain complete and accurate information as we can carry out biological preparation of the experimental animal; (8) to obtain maximum data for the purpose of simulated research; and (9) to test the experimental animal for safety, diagnostics and toxicity assays.

Several small animals have relatively similar specific characteristics, while others have identical physiological, metabolic processes with those of humans. White rat is often used to determine protein quality, chemical compounds toxicity, and carcinogenicity, and measure pesticides residue quantity after being fed with agricultural products (Fitzpatrick, 2003). There are so-called *3R principles* in using the experimental animals, i.e., replacement, reduction, and refinement. Replacement is that the need of using experimental animals is decided after careful observation and calculation, through past experiences or references in answering the research questions, which cannot be done merely by using cells or tissue cultures. Reduction means that the use of the experimental animal is kept at the minimum possible but with optimal results. Refinement is the need to take the utmost care for the animals, not injure them, and minimize harmful treatment, ensuring animal welfare throughout the research. Ethical clearance should be written on the research report or its publication to show how the research treats the experimental animals (Baumans, 2004; Becker & Cowan, 2009; Bousfield & Brown, 2010; Ridwan, 2013). The experimental animals commonly used in agriculture and animal husbandry are cattle, goats, rats, and insects. The use of insects as experimental animals is considered the best alternative for testing agricultural and health-related materials. Their short life cycles and easiness of rearing make them the most suitable animals for research. Nevertheless, from ethical aspects, the use of insects was not that much discussed. Insects as experimental animals are studied more for their conservation and ecosystem balance roles.

ETHICS IN MICROBES USE IN RESEARCH

Genetics resources from microbe come from diverse microorganisms such as bacteria, archaea, viruses, protozoa, fungus, and yeast. Based on their genetics, microbes were grouped into: (1) wild type (wild lines) of microbe, microbe which is directly isolated from nature through any available microbiological techniques and not those which were produced by genetic modification; (2) transgenic microbes produced through genetic engineering which have added outside/ external genetics information, whose offspring will be able to inherit the traits coming from these information; (3) pathogenic microbes that are microorganisms with pathogenic characteristics and capable of inflicting diseases (Sutanto, 2010).

The microbe has been regulated in biomedical fields based on bioethical principles as stated in Universal Declaration on Bioethics and Human Rights. It is mandatory that in each and every decision related to the general use of microbes, several basic rules must be followed, such as: (1) the use of microbe must honor human pride and rights; (2) the use of microbe should prioritize human welfare and not just for the sake of scientific quest or the benefit of a particular group (or groups) of human being only. Human and environmental securities must firstly be taken into account; (3) the use of microbe must refer mainly to the legality, fairness, and equality in both global and local communities. Convention on Bio-Diversity (CBD) recognizes every country's sovereignty in protecting its natural resources, including its microbial richness. Every country has the same right to share a fair and equitable benefit from exploiting and managing their microbiological natural resources. This kind of sharing has consequences on the accessing right of every country to their biological resources, including the microbes that should be mutually agreed on the material agreement if the exploitation is either bilateral or multilateral between countries (Koesnandar & Helianti, 2008; Thomas & Miller, 2017).

The use of microbes should consider and not damage the environment and microorganisms' biodiversity, which means that their use and exploitation should protect the need of the following next generation, who will demand a healthy environment and natural resources richness. The application of genetic engineering on microbes should not be harmful to the environment and decrease sustainability, such as (1) affecting ecological balance, which can be dangerous to human health and, for broader scale, nature; (2) destroying organisms which indirectly affect biodiversity; (3) giving rise to newer problems; (4) inducing a change in food composition on and the ground and the geochemistry process therein. These rules are generally also applied to agricultural research, mainly in agricultural biotechnology and genetic engineering (Sutanto, 2010; Cowan, 2015).

GLOBAL STATUS AND TRANSGENIC PLANTS CONTROVERSY

Crop engineering products and technology are considered solutions with an excellent prospect in fulfilling the scarcity of food and other human needs from the agricultural sector. Genetic engineering technology can create transgenic crops with newer characters and traits, hopefully increasing production capacities and plant nutrient deficiencies and environmental stress (Tolin & Vidaver, 2009; Chaturvedi *et al*., 2016).

In the last two years, developing countries planted more engineered plants than industrial countries. Out of 29 countries that planted transgenic crops, 24 were developing countries, and 5 were industrial countries (James, 2014; Cowan, 2015; International Service for the Acquisition of Agri-biotech Applications [ISAAA], 2020). Countries like Bangladesh, Pakistan, and Vietnam started planting transgenic crops in 2015 (Jefferson & Padmanabhan, 2016). Currently, the total area planted with transgenic crops had reached 190.4 million hectares, and the crops were planted on a large scale in Argentina, Brazil, Canada, China, India, Pakistan, and the United States of America

(Fontes, 2003; Watanabe *et al.*, 2004; Jefferson & Padmanabhan, 2016; Si & Zhao, 2016; ISAAA, 2020). Transgenic crops planted including soybean, corn/maize, canola, cotton, rice, and several others. Aside from fulfilling domestic needs, transgenic crops products are also crucial as export commodities such as food, feed, and industrial raw materials. Several research activities on genetic engineering in Indonesia including pest resistant corn, pest diseases and moisture resistant rice, viral disease tolerant groundnut, moisture-resistant sugarcane, fungal disease-resistant potato, low saturated fat content oil palm oil, pest resistant and high nutrient soybean, and pest resistant sweet potato (Sunarlim & Sutrisno, 2003; *Balai Besar Penelitian dan Pengembangan Bioteknologi dan Sumberdaya Genetik Pertanian* [BB Biogen], 2016). Until 2019, Indonesia has approved 27 genetically modified organisms (GMOs), including agricultural commodities such as soybeans, corn, sugar cane, potatoes, and various vaccines for chickens. Drought tolerant sugarcane has been planted in limited areas in Indonesia belongs to a state-owned agricultural company (PTPN XI) (Bahagiawati & Hadiarto, 2020).

Transgenic crops potency as a solution to increase the productivity of the agricultural sector is beyond doubt. Still, in practice, the crops which were being developed were those with the possibility of bringing great profit to biotechnology growing companies. Ideally, transgenic development should be directed to produce crops resistant to extreme environmental conditions and then made accessible to all farmers level (Uzogara, 2000). Nevertheless, the fact remains that transgenic crops are often designed to suit large-scale agricultural enterprises and are difficult to be applied on small scale agriculture. It is a phenomenon caused by biotechnological developers' tendency to create more economically profitable products rather than accommodate the need of today's agriculture.

The GMO controversy is also related to possible risks to various aspects of public life such as health, environment, religion, culture, and ethics. In agriculture, genetically modified crops have the potential to disrupt the balance of the ecosystem. Another problem is the possibility of killing other living things such as Lepidoptera larvae and microorganisms in the soil. This will impact the quantity and quality of crop production (Mahrus, 2014; Wasilah *et al.*, 2019).

Genetically modified food is thought to be the cause of various diseases on the assumption that foreign genes might change the nutritional value of food in unexpected ways. Additionally, many GMO foods with potential allergies are unknown or untested. Genes from non-food sources and new gene combinations can trigger allergic reactions in some people who consume them (Nordlee *et al.*, 1996). Indonesia is an importer and consumer of GMO products, such as soybeans processed into "tahu" and "tempeh". Muslim communities in Indonesia, as the majority group, have provisions that require halal and good food to be consumed. Labeling the contents of GMO food products is very important.

ETHICS IN TRANSGENIC CROP ENGINEERING

The talk about ethical aspects of genetically modified organism (GMO) creation is based on two critical aspects, i.e., intrinsic and extrinsic. The first aspect states that GMO creation is in itself an unnatural process. This inherent aspect has also based the opinion that GMO creation may not be tolerated as it interferes or disturbs the natural process (Daño, 2007; Bhumiratana & Kongsawat, 2008; Weale, 2010). There is four main intrinsic aspect opinion which rejects the existence and the use of GMO. The first says that changing any living organism's fate through genetic engineering is similar to playing God. Those with this opinion state that genetic engineering is interfering with the natural process, which is the realm of God; therefore, the process is theologically unethical (Amin *et al.*, 2011). This statement is countered by those who stated that this opinion is not rational and that genetic engineering will take agriculture back into the natural system. GMO is claimed to decrease the use of agrochemicals and increase biodiversity, even if it can regenerate marginal agricultural land with natural vegetation (Zadoks & Waibel, 2000). The second opinion states that newer genetic engineering and technology may change nature and the whole world, something which exclusively under the absolute command of God. The third opinion says that genetic engineering blurs the species concept and erases boundaries between species by removing and transferring genes from one species to the others (Lu & Yang, 2009; Ankeny, 2017). The fourth opinion states that the species which undergo genetic transfer will suffer. In general, these intrinsic opinions are rooted deeply in egocentrism and personal fanaticism born out of religious and spiritual beliefs, which makes them almost impossible to change (Bhumiratana & Kongsawat, 2008; Cowan, 2015).

The second aspect is an extrinsic one which is based on the hazard potency and the damage that may arise from the use of GMOs. The negative impact of worrying the public about GMOs is the negative impact on the environment and human health (Rustiawan & Vanda, 1990; Kelly *et al.*, 2010). Transgenic crops may contaminate the environment by cross-pollinating individual non-transgenic plants and may disturb genetic diversity (Arcieri, 2016; Hoffman, 2016). GMO products, especially those designed for human consumption, may bring about allergies and diseases to humans who consume them (Batista *et al.*, 2005; Bhumiratana & Kongsawat, 2008; Holst-Jensen, 2009; Morandini, 2010).

Another worrisome impact is its market. Small scale farmers may be pushed aside by large-scale agricultural enterprises that can plant GMO crops in such a magnitude that they may fully control market price and its policy without any consideration to smaller farming (Hake *et al.*, 2016). It will appear beneficial only to those with such power and will phase out small enterprises. The best solution to answer this extrinsic aspect is by preparing carefully and legally binding rules and regulations on using and developing GMOs, whether environmental damage, human health, or economic disruption, can be contained justly and fairly.

GMO crops have potential risks to the environment when widely cultivated. Agricultural cropping patterns in Indonesia are generally carried out in small areas surrounded by various weeds. With the cross-pollination nature of GMO crops, there is a risk of new weeds being more resistant to herbicides (Mahrus, 2014). Losey *et al.* (1999) reported higher mortality in monarch larvae when fed milkweed (their natural food supply) covered in pollen from transgenic corn than when fed milkweed from regular corn. The report was also followed by the publication of Hansen Jesse and Obrycki (2000), suggesting that the natural levels of Bt corn pollen in the field were harmful to monarch larvae. Another risk of particular concern relating to GMOs is the risk of horizontal gene transfer (HGT), competition with natural species, and increased selection pressure on target and non-target organisms, including non-target secondary pest outbreaks (Prakash *et al.*, 2011). GMO development is a two-sided knife. One side creates hope, and the other brings about adverse effects. The problems arise in ethical, legal, and social areas of GMO use. More research and studies are needed in these areas so that GMOs may be developed for the welfare of the general public and the community (Bhumiratana & Kongsawat, 2008; Urker *et al.*, 2012).

GENETICS ENGINEERING PRODUCTS REGULATING POLICIES

An effort to prevent the negative impact of GMOs use could be carried out by applying rules and regulations on the management and usage of GMOs. All the concern about the disappearance of biodiversity caused by mixing GMO and non-transgenic organisms aroused international-scale discussions and talked to lessen the risk of this negative impact (Howlett & Mukherjee, 2016). The international rule which regulates GMO implementation that may endanger biosafety is known as Cartagena Protocol on Biosafety. More than 120 countries participated in this protocol (Fontes, 2003; Watanabe *et al.*, 2004). This rule is aimed to ensure GMO transfer mechanism, management and usage, products of biotechnological activities which may bring about adverse effects on the conservation and biodiversity functioning in the long term (Dunwell, 2003), and its risk toward human health (Pertry *et al.*, 2014). One of the countries that had adopted this regulation since 2004 is Denmark. The Denmark administration ceded a law which regulate permit system in growing transgenic plants/crops, safe distance isolation procedure that has been scientifically analyzed and amended, and also a regulation which describe responsibility procedures toward damage and disturbance which may arise from the mixing of transgenic and non-transgenic organisms (Watanabe *et al.*, 2004; Varzakas & Tzanidis, 2016). Clear and descriptive labeling on genetics engineering products should also be implemented (Syaifuddin & Handayani, 2013; Preston & Wickson, 2016).

Guidelines on the study of the food security of the genetics engineering products in Indonesia has been written by the Technical Team of Biological and Food Securities based on Joint Ministerial Decree of the Minister of Agriculture, Minister of Forestry and Estate Crops, Minister of Health, and State Minister of Food and Horticulture No. 998.1/Kpts/OT.210/9/99; 790.a/Kpts-IX/1999; 1145A/MENKES/SKB/IX/1999; 015A/Meneg PHOR/09/1999 on Biological Security and Genetical Engineering Agricultural Food Products Security. This guideline consists of requirements and procedures of food security studies, requirements and procedures for genetic engineering food product security, and decisions concerning genetic engineering food product security. The regulation on the genetic engineering products biological security can be found on Governmental Decree No. 21/2005 about Genetic Engineering Products Biological Security (BB Biogen, 2016). The implementation of the release of plant seeds or seedlings is regulated in the Regulation of the Minister of Agriculture No. 37/Permentan/OT.140/8/2006 concerning Testing, Assessment, Release, and Revocation of Varieties. Regulations regarding Guidelines for the Assessment of Food Safety for Genetic Engineering Products are regulated in Regulation of the National Agency of Drug and Food Control No. HK.03.1. 23.03.12.1563/2012.

The implication and implementation of these rules and regulations must be in line with the goal and aims of genetic engineering, especially those concerning food and agricultural products. For research and development purposes, it is expected that there is little leniency in its practice so that the progress and advancement of the existing biotechnology may be rapidly and concisely executed without too much bureaucratic intervention. On the other hand, commercial purposes should be more tightly regulated as they will affect public health and welfare. Even in its development phase, transgenic crops and the commercialization of their products should be thoroughly studied about their monitoring models, risk management scheme, evaluation, and reimbursement procedures should the products inflict adverse aftereffects on society (Watanabe *et al.*, 2004).

CONCLUDING REMARK

Ethics in experimental research include all activities before, during, and after the investigation concerning personal, research, and social ethics. The code and policy of ethics in conducting research include honesty, objectivity, integrity, vigilance, openness, honoring intellectual property, confidentiality, responsible publication, mentoring responsibility, social responsibility, competency, legality, and protection in utilizing living organisms (plant, animal, human) as the object/subject of the research. One particular development that becomes controversial in an ethical sense is the advance and introduction of agricultural biotechnology and the genetic engineering process. Many regulations regarding GMOs have been made in Indonesia. However, the implementation and monitoring of these regulations are not yet precise. It is necessary to consider an excellent and comprehensive discussion involving all sectors related to GMOs in Indonesia. The unclear and ineffective rules need to be reviewed. The implementation of these developments must be ensured to prevent environmental hazards, human health, and the economic system because of this progress in Indonesia.

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