

**Review of Taleb et al., The Precautionary Principle (with Application to the Genetic Modification of Organisms)
(27 November 2014)**

In this manuscript, the authors consider the application of the precautionary principle (PP) to genetically modified organisms (GMOs). They start with the understanding that the PP mandates that if there is suspected risk of irreversible ruin, or severe harm, to the public domain, then the proposed activity should not be pursued absent “near-certainty” about its safety. Further, they posit that PP should be applied to activities that are likely to result in “systemic”, rather than “local” effects. The results of such systemic effects could be as severe as extinction of all life on the planet. After applying a statistical analysis, in which they consider the properties of complex systems, they conclude that PP should be applied to GMOs, as they have the potential to cause such global harm. In particular, it is intimated that development of plant varieties using GMO methodology involves more risk of leading to ruin than development of plants using conventional breeding techniques.

The application of PP requires an initial understanding of the knowledge base surrounding the system that is under examination. To consider the application of PP to GMOs, it is necessary to first evaluate the biology, so that the input is defined appropriately. This review considers the biological aspects of the manuscript.

1. In Section IV D. Distinguishing Global and Local Risks, it would be very helpful to provide an example or citation to illustrate how scientific analysis is able to distinguish global or local risks, and how it is determined whether global harm is probable. Are there examples of mechanisms that could be involved?
2. In Section X B., GMOs are introduced as being the subject of debate. A definition of GMO should be provided here. Does the definition include transgenic, cisgenic, genome engineering, protoplast fusion, induced polyploidy, interspecific hybridization and/or mutation breeding? Is there justification for what is included and what is excluded under the moniker of “GMO”?
3. A citation should be provided to support the statement that “GMOs have the propensity to spread uncontrollably”.
4. Adverse human health effects linked to the process of genetic modification have never been reported. Human feeding studies lack a hypothesis to justify.
5. The statement “The widespread impacts of GMOs on ecologies and human health imply they are the domain of the PP.” requires supporting citations.

6. In Section X B., and illustrated in Figure 8, monoculture is conflated with GMO, when they are in fact independent of one another. Evidence needs to be provided to support any links between use of GMO methods and monoculture. It is well known that monoculture can be, and is, practiced without GMO.
7. Invasive species, by definition, enter ecosystems that have evolved in their absence. It is therefore puzzling that the authors suggest that “long term evolutionary testing of harmful impacts of organisms on local ecological systems mitigates if not eliminates the largest possible risks.” This statement needs clarification.
8. Breeding involving GMOs is compared with “selective farming our ancestors have been doing for generations”, when it should more properly be compared to conventional breeding programs that do not implement GMO methods.
9. An example is provided, of putting a fish gene in a tomato, and suggesting that such a process is outside of natural selection. The implication is that non-GMO crop breeding methods are subject to natural selection only, and no artificial selection. This has never been true throughout the history of crop breeding, as, by definition, the selection has been carried out by humans. Crops are not bred, nor cultivated, solely within natural systems.
10. It is stated that “pesticide resistant crops are subject to increased use of pesticides, which are subsequently present in the plant in larger concentrations and cannot be washed away.” This assertion requires a citation. Available data indicates the opposite of what is stated (Klümper W, Qaim M. 2014. A Meta-Analysis of the Impacts of Genetically Modified Crops. PLoS ONE 9:e111629.)
11. If PP is applied to GMO plants, owing to a risk of ruin, then should not PP also apply in a similar manner to non-plant GMOs? If not, why not?