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ARTICLES

Some Basis for a Renewed Regulation of Agri-Food Biotechnology in the EU

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Abstract A radical reform of the agri-food biotech regulation in the EU is considered in many quarters (mostly by academia and industry) as a pressing necessity. Indeed, two important decisions (by the European Court of Justice and by the Commission) on the legal status of the so-called New Breeding Techniques are expected shortly. In order to clarify some basic aspects of the complex scenario, after a brief introduction regarding the ''GMO'' fallacy, we offer our point of view on the following facets: (1) A faulty approach is frequent in the discussion of the agri-food regulation; (2) NBTs, genome editing may lead to the disappearance of the ''GMO'' meme; (3) Beyond health and safety issues: socio-economic considerations; (4) Sustainability: the comprehensive, meaningful starting point of a positive reform; (5) The theoretical and legal basis for the reform are already contained in the EU's general guidelines to legislation.

To the Editor: We would like to start from a paper recently published in this journal (Zetterberg and Edvardsson Björnberg 2017; from now on Z-EB) to offer some constructive criticism and give a provisional outline of a wider hypothesis regarding the necessary radical reform of the agri-food biotechnology regulation in the EU. We hope that this letter, published in an authoritative social/human sciences journal, may attract the attention of scholars outside the life sciences field, where most concepts that we will try to explain are taken for granted—whereas the message, in our opinion, has not yet fully reached other scholarly areas. To put it more bluntly, as far as advanced innovative biotechnologies are concerned, ''[s]ocial science disciplines have played an important, but not always impartial, role in understanding these changes, […] questioning the authority of scientific expertise and the validity of scientific evidence used to support policy and regulatory decisions by government'' (Tait 2016, p. 7).

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Introduction: ‘‘GMO’’ is a Fallacious Non-category

The expression ‘‘genetically modified organism(s)’’ or ‘‘GMO(s)’’ was coined as a shortcut to indicate several agri-food products (mostly crops), which are created using different methods to slightly modify their genetic makeup (to ‘‘recombine’’ or ‘‘splice’’ one or a few sequences of their DNA), often—but not always—adding genes taken from other species (transgenesis). This is done through various techniques in direct and—more or less—targeted ways, in order to cancel undesirable characteristics (i.e. allergenicity or toxicity) or to add useful traits (e.g. resistance to pests, herbicide tolerance, improved nutritional properties, better performance under abiotic stress such as flooding, drought, heat and climate changes). Thus, such ‘‘recombinant DNA’’ (rDNA) processes and products are part of the agri-food, or ‘‘green’’, biotechnologies.

But the term ‘‘GMO(s)’’ is scientifically meaningless and semantically dubious. (1) It is arbitrary, insofar as it does not cover many rDNA products which belong to the areas of ‘‘red’’ (pharmaceutical) or ‘‘white’’ (industrial) biotechnologies, e.g. insulin or enzymes for detergents, produced by genetically engineered bacteria; and even ‘‘green’’ products such as some food ingredients (e.g. chymosin for making cheese), are excluded, without justification, from the ‘‘GMO’’ perimeter. (2) It is inconsistent, because the same traits (e.g. herbicide tolerance) can often be obtained via techniques of genome alteration (e.g. tissue culture, wide crosses, mutagenesis) which are not pigeon-holed under the ‘‘GMO’’ umbrella. (3) The watershed between what is a ‘‘GMO’’ and what is not is blurred, shifting and confused, because new techniques are advancing at a fast pace—think of the ongoing ‘‘genome editing’’ rapid developments (CRISPR and beyond); for instance, transitory states may occur in which a genetic modification is purposely provisional: it is a ‘‘GMO’’, it is not, just in part, only for a while… (4) When products from ‘‘GMO’’ plants are processed, the results are often indistinguishable from the same ‘‘non-GMO’’ products: e.g. syrup, oil, starch from maize or sugar from sugar beets do not contain DNA. (5) Transgenesis is often seen by non-specialists as ‘‘unnatural’’, but horizontal gene transfer is a phenomenon which happens in nature, particularly in the area of plant–microbe interactions: for example, a variety of sweet potatoes contains fragments of bacterial DNA; ironically, such genetic material comes from the same microorganism that is frequently used to attempt the transgenesis (Kyndt et al. 2015. For more than two hundred examples of ‘‘natural GMOs’’, see Tribe 2017).

There is no common denominator to provide a typical ground for so many different products and biotechnological processes: while we can often speak of single transgenic cultivars, there is no such thing as ‘‘GMOness’’ (Tagliabue 2016a).

The ‘‘GMO’’ confused and confusing meme would not be a problem, if it had remained the subject of some vociferous but ineffective anti-biotech propaganda; instead, it has become the basic notion on which entire agri-food regulatory frameworks have been constructed. This wrongheaded perspective can be explained through an in-depth reflection on the (somewhat worn-out) ‘‘process-vs.-product’’ debate.

A Faulty Approach: The Process Versus Product ‘‘False Balance’’

Z-EB show an approach to the discussion that we would call ‘‘law and/or sociology scholars attitude’’, i.e. they examine the subject without questioning whether the very basis of it is scientifically and logically solid or flawed; in relation to the ‘‘GMO’’ complex issue, this limited perspective has been adopted in many papers dedicated e.g. to the Cartagena Protocol: law scholars and sociologists discuss its implementation without even quoting many texts (mostly by life scientists) which have challenged the meaninglessness of the treaty’s rationale. An example of such disposition in relation to the EU ‘‘GMO’’ laws is a paper (Winter 2016) on the recent amendment, i.e. Directive 2015/412 (European Union 2015) of the basic Directive 2001/18 (European Communities 2001): the author examines the subject at length, showing in-depth competence; but he does not consider the idea that the amending regulation is a patch on a dress which is anti-scientific and wrongheaded in itself: in fact, separate regulation of so-called ‘‘GMO’’ has been considered unjustified and detrimental by most life scientists since the beginning.

Among many explicit positions in that sense, consider the plea from the European Molecular Biology Organization, which dates back to 1988, before the 1990 first EU Directive on ‘‘GMO’’: ‘‘EMBO strongly believes that there is no scientific justification for additional, special legislation regulating recombinant DNA research per se. Any rules or legislation should only apply to the safety of products according to their properties, rather than according to the methods used to generate them.’’ (40th meeting of the Council of the EMBO, cit. in Cantley 1995, p. 560). This appeal and many similar ones went unheeded: the EU lawmakers created a ‘‘GMO’’ regulatory ghetto which is still in place. The same ‘‘regulate the product, not the process’’ perspective has been recommended since the 80s in North America: it was implemented in Canada and—only initially and still partially—in the USA.

The EU should give credit to hundreds of scientists that were tasked by the EU itself to make a widespread, in-depth analysis of the scientific status of recombinant DNA (rDNA) agri-food techniques; after a number of research projects during the period 1985–2000, many others were carried out in the decade 2001–2010: ‘‘The main conclusion to be drawn from the efforts of more than 130 research projects, covering a period of more than 25 years of research, and involving more than 500 independent research groups, is that biotechnology, and in particular GMOs, are not per se more risky than e.g. conventional plant breeding technologies.’’ (European Commission 2010, p. 16)

From a scientific point of view, adopting the process, and in particular the rDNA group of methods, as a trigger for regulation of the agri-food biotech area does not make sense: it is the infamous, recurrent error that one of us named ‘‘Genomic Misconception’’ (Ammann 2014). To explain it for the nth time, we will only quote a jewel paper by Nobel laureate Werner Arber: ‘‘conjectural risks of genetic engineering must be of the same order as those for natural biological evolution and for conventional breeding methods. […] There is no scientific reason to assume special long-term risks for GM crops.’’ (Arber 2010, Abstract. For a reference list of many similar positions, see Tagliabue 2016b).

Thus, two opposite regulatory views are possible: (a) to focus on the process(es), i.e. the methods used by breeders in their operations (be they more or less traditional, from classic hybridization to tissue culture, physical/chemical mutagenesis, rDNA operations, New Breeding Techniques, CRISPR and beyond); (b) or, instead, to examine and test the products, i.e. their phenotypes, the actual characteristics of them and their real risk for health and impact on the environment. We support this second approach: in the words of an early paper on the process/product dilemma, we encourage a viewpoint that poses ‘‘no distinction whatever between the treatment of GMOs and other foods, drugs and pesticides’’; yet, particular attention should be devoted to ‘‘any novel hazards that may be suspected’’ (Tait and Levidow 1992, p. 225)—not only from ‘‘GMOs’’, we must add, but from any new agri-food plant, animal or microorganism.

Since the 70s, most life scientists maintain that it is misleading to see the process, instead of the product, as a parameter for regulatory oversight. To be clear, if other groups of products (e.g. those deriving from mutagenesis) were singled out to be governed apart for the sole reason that they derive from certain processes, the rationale would be equally anti-scientific: yet, only ‘‘GMOs’’, in most regulators’ eyes, form a caste that merits unwarranted suspicion.

Note that the adoption of a product-based criterion does *not* mean that the regulation should generally be looser: decision-makers may decide to subject breeders, both in private companies and in public institutions, to lighter or stricter rules (e.g. less or more analytical pre-market tests, in the labs and/or in the fields or farms): but the established guidelines should focus on the different levels of known or rationally foreseeable risks (allergenicity, toxicity, invasiveness), depending on the traits and characteristics of the product (e.g. new varieties of potatoes, due to their biochemical composition, which is possibly prone to toxicity, must be watched more closely than, say, most cereals). Today, instead, any rDNA cultivar is, in almost all jurisdictions, trapped inside a regulatory nightmare which exempts very similar varieties (e.g. mutagenized or hybridized herbicide tolerant sunflowers) that have the same level of risk—be it higher or lower. ‘‘In all of these scenarios involving process-based triggers, limited regulatory resources are expended without any consideration of actual risk and without increasing the actual safety to the public or the environment.’’ (McHughen 2016, p. 131).

The acknowledgement of this early widespread consensus (Tagliabue 2016b) on what are science-based grounds for agri-food biotech regulation should be a necessary keystone of any discussion. So far, it has often not been so on the part of most law students and Science and Technology Studies scholars. In many texts on

the subject, a sort of *false balance* is apparent: regulatory approaches focusing on the process(es) by which agri-food novelties are created (but only if they are pigeonholed into the ‘‘GMO’’ fallacious non-category) are considered equivalent, as far as their legal/sociological analyses are concerned, to those focusing on the products (a science-based view which is agnostic of the origin of them). But any explanation should not forget that opposed regulatory approaches do *not* have the same epistemic value. In situations where the mainstream scientific consensus is clear but challenged by laws or public perceptions, a law expert or sociologist who describes legal and social dynamics will certainly not avoid giving the full background: a law or a widespread social perception which puts vaccines and snake oil on the same level may be ‘‘neutrally’’ analyzed by scholars but, at least as part of the narration, they would include the scientific community’s position. It is not so for ‘‘GMO’’: when existing regulations and public attitudes are illustrated, law experts and sociologists too often are not aware that they have a sort of blind spot for the life sciences stance on the subject—thus justifying unconsciously the years old uncritical use of the present regulatory laws, depending on false premises right from the beginning.

It has been argued that the current regulation of agri-food biotechnologies in the EU[1] (European Communities 2001) is ‘‘both process- and product-oriented’’ because ‘‘the Directive 2001/18/EC contains both process- and product-related terms’’. (Sprink et al. 2016, p. 1494 and 1493) We think that this interpretation is not fully correct: the current EU ‘‘GMO’’ regulation is not a ‘‘hybrid’’ product-process system, but the process (the rDNA origin of the regulated products) is indeed the only trigger which motivated the creation of the ‘‘GMO’’ legal precinct.

In fact, regulators do not impose tests and controls during the actual *process*, i.e. the lab or greenhouse or field works which are operated when breeders attempt to obtain new *products*; there are no legally mandatory guidelines on how to conduct hybridizations or tissue cultures or physical/chemical mutagenesis or the creation of rDNA events. Current process-based frameworks do not dictate that experimenters are controlled during the various steps which lead to the ‘‘prototypes’’ of a promising new product that will be put on the lab table to assess its safety, or tried in the experimental fields to check its possible invasiveness. In fact, they are actually regulating the *product* after all: but they want the phenotypic characteristic of the outcomes to be examined *insofar as they have been obtained through certain processes*, which are—unwarrantedly—considered ‘‘risky’’, i.e. prone to result in unsafe/noxious outcomes. Thus, this is the actual root of the product-versus-product conundrum: frequently biased regulations impose restrictions on certain new organisms (products) *just because they are rDNA* (process).

This important point can be further explained using an analogy, a thought experiment. Via physical/chemical mutagenesis, 3000? varieties have been created (FAO-IAEA 1950–2016), both crops and ornamental: these genome-scrambling techniques have been used since the 50s (see Dick and Jones 2012), without social

[1] To be more precise, the reference here is to the ‘‘deliberate release into the environment of genetically modified organisms’’ (title of Dir. 2001/18), i.e. the *cultivation* of rDNA crops, as opposed to the *use/importation* of them (or their derivatives, or products which contain them as ingredients), which falls under Regulation 1829/2003 ‘‘on genetically modified food and feed’’.

opposition and explicitly excluded from regulation for purely political reasons. Imagine that the anti-biotech movement had surged some decades before, successfully attacking and smearing those methods and successfully hampering them, convincing politicians to restrict their use by law and influencing the gullible or cynical media with frightening messages and scaring images: on their part, scientists would have to try to explain that there were no inherent risks in the outcomes of those innovative experiments. Now, suppose that law scholars and sociologists discussed the legal/social phenomenon, basically without questioning, or even omitting to underline, its anti-scientific bias: that would be a limited, misleading depiction. Fortunately, such a scenario did not materialize for crop mutagenesis; unfortunately, that has been—and still is—the sad story on another group of green technologies: ''GMOs''.

This is not to say, as some over-confident life scientists occasionally claim, that ''the rDNA technology is safe'': no technology, in any field, can be declared to be inherently devoid of risks. Yet, we do not need preliminary, impossible certainty about the infallibility of this or that ''green'' biotech method: because, when a tryout—*''GMO'' or otherwise!*—proves to be unsatisfactory, it is discarded; that is exactly what experimenters have done in various cases, ditching ill-fated rDNA varieties (e.g. soybeans, barley, canola, maize, potato, rice, wheat, flax, corn, etc.) and traditional ones (e.g. squash, celery, and potato) (Haslberger 2003, p. 740; Kuiper et al. 2001, p. 516; Colorado State University 2004). For breeders—now as in the past, and all the more so in the future—the results of any attempt to create new races or varieties must be assessed a posteriori: sets of reliable lab tests, such as those provided and governed by the Codex alimentarius (an institution linked to the World Health Organization and the Food and Agriculture Organization) and similar science-based authorities, are in place.

This confirmation of the correctness of focusing on the single products, obtained via any method, to be examined case by case, may hopefully be seen as the last nail in the coffin of the process-based approach to regulation. (Tagliabue 2017b).

Fortunately, a rational approach has been in place for decades, and it may serve as an example for a meaningful reform in the EU: ''Canadian legislation targets 'plants with new traits' [PNTs], that is, plants containing traits that are both new to the Canadian environment and have the potential to significantly impact on the environment or human health.'' (Z-EB, p. 2) A key point, Z-EB immediately specify, is that ''[t]he traits can be introduced by genetic modification or conventional breeding techniques.'' Such a radically oriented product-based view is the only scientifically defendable framework for regulation.

Now it should be clear that the question asked is inadequate: ''What Legal Principles and Criteria Should a Regulatory Framework for *GMOs* Meet?'' (Z-EB, p. 3, our emphasis). Replace ''GMOs'' with ''new agri-food products'' and the question will be the right one.

NBTs, Genome Editing and the Disappearance of ‘‘GMO’’

In recent years, a number of advanced methods of intervention for modifying and improving living objects has been developed, with important applications also in the ‘‘green’’ sector: a brief explanation of their properties is not feasible, since many esoteric technicalities would have to be discussed; obscure terms and acronyms are involved, e.g. cisgenesis, TALENs, zinc-finger nucleases, reverse breeding etc. Collectively—although a precise list cannot even be agreed on by experts, for reasons that we will now explain—they are named ‘‘New Breeding Techniques’’, ‘‘NBTs’’ (see EASAC 2015; for in-depth descriptions, see European Commission, Scientific Advice Mechanism 2017, pp. 56–75); some of these techniques, also according to details in their different applications, may be indicated also as ‘‘gene editing’’ or, better, ‘‘genome editing’’. In certain cases, these interventions create transgenic organisms, i.e. some sequences of exogenous coding DNA are permanently infused in the genome of the new organisms (only the methods differ from those used in ‘‘classic’’ transgenesis); in other situations, the insertion is only provisional, in that it is useful during the lab work (the resulting phenotype is not transgenic); or there is not an insertion but a deletion of nucleic acids: or the genome is not changed, but epigenetically influenced, so to say, in order to ‘‘switch on or off’’ certain genes; in these three last occasions, the new organisms are indistinguishable from those deriving from artificial (e.g. crossing, physical/chemical mutagenesis) or natural mutations.

Note that we refuse the inadequate adjective ‘‘foreign’’ DNA, as if the inserted snippets of nucleotides were something alien. In genetics and biology, bases are bases and genes are genes; they may be found in the same exact sequence in organisms which are phenotypically quite different, and taxonomically very ‘‘far’’ on the tree of life: if we manage to copy and paste into an organism a gene that is found in another, and it produces the protein and trait we need, that is the marvel of transgenesis—which may also occur in nature, although not often: it is called Horizontal Gene Transfer.

The contorted story of the (not yet assessed) legal status of the NBTs in the EU has been told elsewhere (Tagliabue 2016a): suffice it here to say that a Working Group of experts, which was created by the Commission in 2008, produced a final report in 2012, but no decision has been taken on whether these methods should be considered ‘‘GMO’’ and therefore fall inside the scope—we may say: the trap—of the related regulation, or be excluded. In the meantime, the CRISPR revolution is exploding, also with very interesting perspectives for the agri-food areas—i.e. another powerful NBT, or genome editing tool, is being created (Hall 2016). Furthermore, ‘‘other NBTs will likely be developed in the future in which case the problem of legal uncertainty resurfaces. There is, in other words, an inherent vulnerability in a legal construction that regulates risk based on the use of a specific technology and where the boundaries of the technology are in need of continuous redefinition due to rapid advancement in science.’’ (Z-EB, p. 9) Inevitably, the still unpublished report of 2012 is already outdated: amend it, and it will be outdated in a short period—and so on, in a useless spiral.

We need to be repetitive: this messy quandary is another confusing consequence of using a process-based regulatory approach. Worse, a wrong question is asked, i.e. whether this or that NBT produces ‘‘GMOs’’ or not: the answer is supposed to allow decision-makers to place it under the present regulatory umbrella or not. The rapid exit from such an age-old maze is incredibly simple: breeding techniques (the processes), present and future, new or old, traditional or not, are an inadequate, misleading trigger for agri-food biotech regulation: a brand-new start would consider the single organisms, i.e. their actual characteristics (the product), however modified (as already asked bluntly in Ammann 2014). If a possibly astonished reader is wondering whether we are proposing to evaporate the same notion of ‘‘GMO’’ from the EU regulation, the answer is: yes. While life scientists and some epistemologists have tried to explain many times that the pseudo-category of ‘‘GMO’’, apart from its dubious semantic status, is scientifically nonsensical and detrimental for regulatory purposes, we hope it is time to remove this fallacy also from the human/social science areas and, even more so, from agri-food biotech theory and rules: the ‘‘GMO’’ paradigm must be broken, because it has been a gigantic historical, cultural and intellectual blunder, that should be stopped from getting in the way of a rational debate—above all in the green biotechnology area. The eradication of the ‘‘GMO’’ legal and political weed would not imply any diminishment of the necessary precaution, neither jeopardize the reliability of a sound, logically tiered regulatory framework; just the opposite: ask brainy Canadians, who have never got imprisoned in the ‘‘GMO’’ iron cage (Smyth 2014).

Beyond Health and Safety Issues: Socio-economic Factors

It has been argued that a meaningful reform of the EU agri-food biotech regulation should include, beyond the necessary provisions regarding the basic health and environmental safety of the products, also socio-economic concerns (non-safety considerations) regarding the impact of the new scientific and technological developments. Generally speaking, the request to broaden the approach seems reasonable, on ethical and political grounds.

The problem thickens if we think that regulations should also ‘‘be responsive to people’s political, ethical, and religious beliefs and preferences concerning food production, retailing and marketing’’ (Z-EB, p. 6): what if supporters of freely accepted diets or behaviors (e.g. Halal, Kosher) or enemies of certain products (e.g. alcohol, meat) demand that their habits be considered by lawmakers as *exclusive* rules? The problem with special regulations regarding certain foods is not their fiscal treatment or legal rules aimed at ‘‘fine tuning’’ their consumption: incentives and disincentives (e.f. sugary drinks tax) or even mandatory limits (e.g. alcohol for minors, drivers) are not a denial of the free market framework. Instead, sweeping bans or forceful food guidelines (e.g. complete prohibition of meat) would be dubious impositions. In democratic societies, governed as regulated free markets, the preferences of groups can be expressed, also in terms of consumer choices, but such orientations should not become rules for everybody.

That's why the insertion of socio-economic factors into agri-food laws is a complex problem, because—a point which is missing in Z-EB—it may create frictions at the World Trade Organization level, i.e. clash against the international agreements on free trade, as far as non-safety law provisions are seen to involve, or to mask, protectionist intents. In fact, the EU has already lost a dispute in a transatlantic case, raised by Argentina, Canada and the USA against a moratorium of ''GMO'' in the Old continent which lasted some years (Bernauer and Aerni 2008): since the current trade treaties do not consider socio-economic issues, the EU tried to base its botched counter-argument on indefensible motivations regarding alleged health risks of ''GMOs''. Resorting to groundless safety speculations may be seen as an inconsistent attempt to affirm legitimate socio-economic concerns that otherwise would not find any space in the existent framework. Therefore, in our opinion, a possible future reform of the current international trade regime should open to some wider perspective: this goal may be achieved by renegotiating the trade agreements, as many commentators have proposed.

Indeed, any consideration regarding the place of socio-economic issues in the regulatory framework of agriculture—both at national and international level—must abandon the ''GMO/non-GMO'' misleading watershed.

We can explain this by briefly discussing a non-safety issue which is often cited as a negative characteristic of modern-industrial agriculture, frequently linked to the ''GMO'' notion: the prevalence of monocultures. Yet, for better or worse, extensively cultivated single crops can exist without being genetically modified (e.g. bananas, in many countries; oil palms, in South-East Asia); they can be pre-existing, and only subsequently be DNA-spliced to add a significant trait (e.g. alfalfa, an widespread herb for fodder, which has been made tolerant to herbicides in the USA (http://en.wikipedia.org/wiki/Alfalfa#Genetically_modified_alfalfa). All else being equal (e.g. property rights), these existing crops do not change their social impact if we add a useful trait through a slight readjustment to their DNA, making them ''GMOs''. A narrow focus on the rDNA origin of cultivars impedes a wider com- prehension of the agricultural world, especially as far as biodiversity is concerned. A link to the current ''GMO'' legislation may clarify this important question.

Directive 2015/412 (European Union 2015) amends the basic ''GMO'' Directive 2001/18 (European Communities 2001) by adding two new articles, Article 26b and Article 26c. The European Food Safety Agency remains the sole body in charge of the environmental and health assessment (safety issues) of ''GMOs'' at EU level, but Member States are allowed to prohibit the cultivation of approved recombinant DNA varieties at a national or even local level, based on extra-scientific grounds (non-safety issues), e.g. ''environmental or agricultural policy objectives, or other compelling grounds such as town and country planning, land use, socioeconomic impacts, coexistence and public policy'' (European Union 2015, Preamble, 13. See also Art. 26b, point 3). Note that such restrictions may apply to the *cultivation* of rDNA varieties; only one cultivar has been approved (maize MON810), but its availability to farmers has been impeded for many years in most EU countries with legalistic quibbles and complete bans: the Commission and the EU Court of Justice have underscored in various occasions that such behaviour by Member States is illegal, yet the approach has persisted. On the other side, the *use*, i.e. importation, of

‘‘GMO’’ commodities in the EU (mostly maize, soybeans and cotton) is massive—several million tons every year: the list of approved genetically engineered crops comprises several dozen items. Thus, ‘‘GMOs’’ are safe, but only if imported, not raised in the EU. As we said, the amending Directive 2015/18 is just a patch on a legally inconsistent framework: as commentators have pointed out, the WTO sword of Damocles is still hanging (For a thorough dissection of the current ‘‘GMO’’ legislation in the EU, see Tagliabue 2017a).

But our intent here is to explain why focusing on ‘‘GMOs’’ and allowing restrictions of their cultivation is both illogic and detrimental. The list of non-safety issues which should justify forbidding European farmers access to rDNA seeds is only apparently reasonable, but a minimal reflection shows an obvious contradiction. Consider environmental or agricultural policy objectives, town and country planning and land use: these are legitimate and necessary political actions, yet have nothing to do with ‘‘GMOs’’; in fact, if the planning schemes foresee that a certain area is going to be cultivated, the permission to grow cereals or legumes or any other crop has no link with the origin of the varieties that farmers will use. In other words: if planners decide that here we will have huge fields of maize, or small plots of different vegetables, or vast orchards with various fruit trees, why should these decisions prohibit the use of, say, mutagenized cultivars, or in vitro multiplied clones, or grafted plants, or… ‘‘GMOs’’? The claimed link between genetic engineering and environmental/land planning (e.g. extensive monocultures) is not at all necessary and clearly unscientific, and where there is such a link it is banal, i.e. the correlation does *not* influence the given scenarios. Plain and simple: if politicians want to allow or instead restrict the cultivation of vast fields of whatever crops, they have every right to do so; yet, what is the difference if the cultivated or restricted seeds are rDNA or otherwise?

If anything, the difference may be positive. Speaking of non-safety issues, many studies have showed that cultivating ‘‘GMOs’’ instead of old-fangled cultivars brings strong economic benefits, above all to small farmers, above all in the poorer countries—if and where prohibitionism is not enforced by laws: in 2013, 18 million farmers, 90% of whom are smallholders in developing countries—7.3 million in China and 7.5 million in India (James 2014)—raised ‘‘GMO’’ crops. How can low-income farmers afford the price of better seeds? Because their increased revenues justify higher costs: ‘‘even though companies like Monsanto, Pioneer-DuPont, and Syngenta own patents and charge farmers royalty fees for use of the technology, they are only able to capture a minority portion [33 percent on average] of the total economic value they helped to create.’’ (Graff et al. 2014) Thus, in-depth and accurate economic analyses destroy the myth, so common in certain academic quarters and among the public, that ‘‘GMOs’’ are suitable only for bigger agricultural players. Two plus two makes four, and also the poor can do the math. Remember that we are not singing the praises of rDNA cultivars as if they were the silver bullet: sometimes, non-transgenic outcomes perform better (Gilbert 2014); if completely ‘‘non-GMO’’ solutions were available and worked more effectively, all else being equal, economic operators would quickly embrace them, abandoning ‘‘GMO’’—and unbiased academics would acknowledge the progress. Sociologists should eventually endorse the documented and peer-reviewed evidence regarding

the relatively benign non-safety impacts of ‘‘GMOs’’, offered by colleagues in close scholarly areas, i.e. economists. If someone can give different explanations of so many low-income farmers’ choices, those explanations would most probably rely on ‘‘alternative facts’’ (as discussed in Ammann 2013).

On the other hand—and more importantly—the misunderstanding of considering ‘‘GMO’’ as the source of negative societal impacts, and therefore insisting in frustrating the rDNA technology, brings with it dire consequences. There are numerous small local and typical crops (mostly fruits and vegetables), for which genetic engineering solutions are possible—sometimes already available—to protect or improve them in various ways; many are still not applied due to the excessive costs linked to the regulatory nightmare which oppresses ‘‘GMOs’’ (Miller and Bradford 2010). Genetic enhancement can allow the saving of numerous local crops, as has already happened with papaya in Hawaii and may happen with Italian tomatoes and apples; in Europe, there are precious plant varieties which are attacked by various pests (viruses, fungi, insects) against which traditional remedies do not work; many typical products are heading towards extinction and could be saved if some common sense buried the ‘‘GMO’’ mind-polluting frame, leading to a reassessed agri-food regulation.

The research regarding these minor crops is carried out in university and public institutions, because Big Ag, due to the cost of taking a ‘‘GMO’’ to the market, is not interested in smaller revenues (see Ammann’s foreword to Gressel 2007). But the same regulatory tunnel, and above all the difficulty or impossibility of running field tests, make it unfeasible for public scientists to pursue their targets. So, direct and tailor-made genetic improvement to ‘‘secondary’’ crops can help conserve small farm businesses, biodiversity and natural environments in significant ways. But the EU agri-food legislation does not allow that—because those saved crops would be ‘‘GMO’’. How illogical is this?

Moreover, the creation of plants which require little water, or grow on saline terrain, or have increased yields, ensures that more food is produced with fewer resources, or on soil of limited ecological value, so that less virgin areas are given over to farming. And those crops—any crop, actually—could be raised ‘‘agro-ecologically’’ or ‘‘organically’’. Farmers would not care whether the prototypes of those precious new cultivars are created through one or another DNA-tinkering method. Again, focusing on the process(es) instead of the products (in a broader sense, i.e. considering also their social and economic correlations, beyond basic safety) does not make sense—and it is a counterproductive approach. There is a growing literature on organo-transgenic approaches (Ammann 2008, 2009; Ryffel 2017).

To summarise: spinning around the ‘‘GMO’’ erroneous notion muds the waters of any productive debate on agriculture—even more so where its socio-economic impacts are concerned. Any necessary consideration must be developed in a ‘‘horizontal’’ way, avoiding a ‘‘vertical’’ approach. This geometric metaphor of a fruitful regulatory framework, as opposed to a detrimental one, can be explained with a reference to the correct questions that should be asked when considering the agri-food area: (1) Do these new products, were they to be authorized, have an acceptably balanced impact on health, the environment and socio-economic

dynamics (irrespective of the methods used by breeders to invent them)? This is a ''horizontal'', wide-ranging view. (2) Were these new products developed using traditional or recent, indirect or direct or whatever genomic-phenotypic enhancing technique? This ''vertical'' angle is myopic and impractical.

What we are pointing out here is *not* a matter of values: alternative policy guidelines on agriculture may encourage very different choices, in a range that can vary from the strictest regulation to the most liberal, free-market attitude. This must be a matter for open discussion, even heated debates: but any orientation is hopelessly misguided if we do not get rid of the deep antiscientific bias that is implied in the ''GMO''-''non-GMO'' irrational divide.

The Theoretical and Legal Premises of the Reform

Z-EB eventually provide what is the best perspective for a reasonable, ethical, balanced reform in the EU: the idea is to ''introduce a new crop legislation based on sustainability criteria that apply to all varieties regardless of breeding methods used. That is, instead of focusing on whether a crop has been developed through genetic modification or conventional breeding methods the legislation would departure from the values that are central to achieving a sustainable development within plant breeding. This […] represents an entirely different regulatory logic, since the primary goal of such legislation would no longer be to merely avoid risk and harm but to achieve a broader set of sustainability goals.'' (Z-EB, p. 18) We can only applaud such a vision!

A British institution, the Advisory Committee on Releases to the Environment, in 2007 outlined an excellent ''legal solution with a matrix-based approach in the form of a Comparative Sustainability Assessment which contains ten criteria for assessing sustainability: management system and inputs required, persistence and invasiveness, biodiversity, water, soils, energy balance, latency/cumulative effects, reversibility of effects, economic sustainability, and social sustainability.'' (Z-EB, p. 19. For the details, see ACRE 2007, pp. 18–19) The last two criteria are somehow problematic; but this interesting hypothesis is the best basis for overhauling the EU agri-food biotech rules.

Inside such a renewed, comprehensive framework, also the concept of ''sustainable intensification in agriculture'' can have a place (Garnett et al. 2013)—while ''GMO'' would be thrown into oblivion.

A radical remaking of the agri-food regulation can be based on the existent theoretical and legal framework. In 2016, the ''three institutions'' of the EU approved the ''Interinstitutional Agreement between the European Parliament, the Council of the European Union and the European Commission on Better Law-Making'', whose primary aims are that legislation is ''as simple and as clear as possible, avoids overregulation and administrative burdens for citizens, administrations and businesses, especially small and medium-sized enterprises'' (European Union 2016, (2)).

These objectives are anything but vague, as they are specified and implemented in the real world: ''REFIT—Making EU law simpler and less costly—The

Commission's Regulatory Fitness and Performance (REFIT) programme ensures that EU legislation delivers results for citizens and businesses effectively, efficiently and at minimum cost. REFIT aims to keep EU law simple, remove unnecessary burdens and adapt existing legislation without compromising on policy objectives.'' (REFIT 2016).

The main document underlines the EU's ''obligation to legislate only where and to the extent necessary'' (European Union 2016, (3)). To our knowledge, there is no sector which has been oppressed for almost three decades by useless red tape more than green rDNA technology: following its guidelines, the EU should scrap any sectoral and sectarian regulation on so-called ''GMO'' and approve a new framework in which socio-economic concerns linked to agricultural biotechnologies are not merely seen in a narrow, *negative* sense (i.e. excuses to impede ''GMOs'' here and there in the territory) but in a broader, *positive* sense (i.e. promoting articulate, credible policies of sustainable scientific and technical development of agri-food progress), even renegotiating the WTO agreements.

Again: levelling the ground for the regulation of plant/animal/microbial novelties (living organisms and products thereof), an action which implies the uprooting of the imaginary—yet very real!—''GMO'' rickety fence, does *not* mean reducing the necessary attention to hazard and risk; instead, it means the application of a logically tiered, science-based precautionary mindset.

A Temporary Conclusion

In conclusion, we are aware that this is just a letter, and therefore its arguments should be more extensively articulated. It is our intention to transform it into a full research paper, but we have to wait for an upcoming (hopefully close) development of the situation, that rests on two foreseen events: (a) the determination of the Court of Justice of the EU on the legal status of some NBTs (the ''mutagenetic'' ones), following a request for clarification that has been submitted by the French Conseil d'État (www.conseil-etat.fr/Actualites/Communiques/Organismes-obtenus-par-mutagenese); (b) the long-awaited orientation of the European Commission on whether NBTs are ''GMO'' or not, which has declaredly been delayed so far also to consider the forthcoming EUCJ stance (www.ombudsman.europa.eu/cases/decision.faces/en/75646/html.bookmark).

We hope that our attempt to clarify some major points of the complex subject and to outline some keystones of a good agri-food biotech regulation will have a positive impact on the ongoing debate for the badly needed reform. We are hopeful.

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