Substantial equivalence and ethical equivalence: contrasting approaches

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The concept of substantial equivalence (SE) was used in the following two successive discussion sessions during the workshop: 1) to clarify the values implicitly incorporated in genetically modified organisms (GMOs), and 2) to explore the possible introduction of complementary equivalence concepts, i.e. qualitative equivalence (QE) and ethical equivalence (EE), to integrate the wider social demand.
Both discussions were preceded by short presentations. In the first session, the definition and purpose of SE were introduced along with scientific objections raised by this concept. To account for objections other than scientific, i.e. the other 'legitimate factors' and values at stake in society, the normative levels and background assumptions implied by SE were then examined. In the second session, a possible way to integrate values in the normative approach and evaluation of food was presented based on the concept of equivalence. Further to physico-chemical properties, quality and values were considered to reveal wider intrinsic properties of organic substance, or 'food substance integrity'. Recognition of these other legitimate factors also pointed to the democratic implications of food evaluation.

1. The history, definition, and scientific controversy about substantial equivalence

SE was introduced in 1993 by the OECD (Organisation for Economic Cooperation and Development) to provide a '*dynamic, analytical exercise*' in the safety assessment of novel foods derived from modern biotechnology, i.e. GMOs, by means of comparison with traditional food. The basic definition was as follows: 'The scientific approach to evaluations [of 'the safe use of new foods or food components'] is based on a *comparison with traditional foods that have a safe history of use*... The Working group considered SE to be the *most practical way to address the issue of food safety* at this time.' (OECD, 1993). The main conclusion of the report was: 'If the new or modified food or food component is determined to be SE to an existing food, the further safety or nutritional concerns are expected to be insignificant. Such foods, *once SE has been established*, are treated in the same manner as their *analogous conventional counterparts*' (OECD, 1993). Although SE is not meant to be a safety assessment in itself but a starting point that is used to structure the safety assessment, it is nevertheless endowed with political authority.
The concept of SE was endorsed by the FAO (Food and Agriculture Organisation) and WHO (World Health Organisation) in 1996. It was implemented by the OECD and by the European Union (EU) in 1997 (OECD, 1998; EC Regulation 258/97). In the 1998 OECD report, the implications of SE are further presented: '*Statistically significant differences* between the genetically modified line and the chosen comparator are *not necessarily indicative of a safety concern* but they may require further investigation.'...'establishing *SE can be used to demonstrate the absence of untoward secondary effects* of a genetic modification and the relative safety of a new food compared to its conventional counterpart. If the comparison shows the absence of untoward secondary effects of a genetic modification, this conclusion will be *equally valid in all countries and for applications* of the modified crops' (OECD, 1998). It thus appears that SE is intended to have full world-wide authority in decision-making and that the presence and absence of SE have unequal consequences in regulatory procedures. Indeed, substantially equivalent foods no longer containing GM protein or DNA, such as refined oils, are only submitted to a light authorisation procedure.

An operational definition of SE was not available when EC regulation 258/97 came into force in 1997 and is still not available. Nevertheless, several GM plants and/or ingredients have been determined SE in the EU (Schenkelaars Biotechnology Consultancy report, 2001). In USA and Canada, all GM crops on the market have been found SE (Clark and Lehman, 2000). The legal implications of SE contrasted with its lack of operational definition have been a major source of controversy in the scientific community. A critical commentary published in Nature in 1999 heated up the debate on SE and had an important impact on the scientific community and on expert committees (Millstone *et al*., 1999; Schenkelaars Biotechnology Consultancy report, 2001). In their commentary, Millstone *et al*. raised a number of important issues. They argued that '*the degree of difference between a natural food and its GM alternative* before its 'substance' ceases to be acceptably 'equivalent' is not defined anywhere, nor has an exact definition been agreed by legislators'. Their main argument was that SE 'is *misguided* and should be abandoned in favour of [an approach] that includes *biological, toxicological and immunological tests rather than merely chemical ones*' (Millstone *et al*., 1999). Whilst the lack of extensive experimental validation is usually the main subject of controversy, the epistemological and deontological premises of SE are usually not questioned. However, Ho and Steinbrecher (1998) stressed that '*SE is based on partisan claims* in favour of genetic engineering [GE]', an argument which is already beyond basic scientific concerns.

The definition of SE has been further explored in FAO, WHO, Codex Alimentarius, and OECD expert meetings in 2000 and 2001. In this context, the Dutch Foundation 'Consument en Biotechnologie' commissioned Schenkelaars Biotechnology Consultancy to prepare a report on international and European regulatory discussions on the concept of SE (Schenkelaars Biotechnology Consultancy, 2001). Besides recommendations concerning the validity of the comparators, trial protocols, list of compounds analysed, analytical techniques and statistical methods of analysis, it was concluded that 'omics' profiling techniques based on genomics, proteomics, and metabolomics should be further developed and validated to address potential toxicological or nutritional unintended effects. However, the FAO/WHO Codex Alimentarius, probably due to the scientific controversy about SE in 2000, also raised the question of the validity and limitations of SE for the safety and nutritional assessment: 'What is the role, and what are the limitations, of SE? Are there alternative strategies to SE that should be used?' (Schenkelaars Biotechnology Consultancy, 2001).

2. The normative levels and background assumptions of SE

In the 1993 OECD report, three main background assumptions about SE are explicitly expressed. Firstly, it is stated that the 'evaluation of foods and food components obtained from organisms developed by the *application of the newer techniques does not necessitate a fundamental change in established principles*, nor does it require a different standard of safety'. In other words, GM foods do not introduce new hazards compared to foods produced by traditional methods. A second postulate is deduced from the first one stating that GM food assessment, including SE, can be extended to any food: 'Knowledge obtained using these methods might also be used to *approach safety assessment of new foods* or food components from organisms *developed by traditional methods*.' Finally, the report introduces a third postulate stating that the concept of SE is not novel in fact and was already embedded in society before: 'This approach is based in turn on the concept of SE, which *articulates procedures used in the past, albeit intuitively*, for accepting new foods.' Whereas the 'intuitive' approach in the past allowed cultural flexibility as to what individuals or societies would consider the right way to address food issues for themselves, the concept of SE imposes one uniform representation of food that is meant to be universal. The report is probably right in saying that SE embodies common, implicit background representation (at least in the countries of the North though this is probably less true in the South). However, it does not say what the basis of this representation is, where it comes from, nor whether other representations exist in the world and also deserve attention.

The concept of SE involves three normative levels. The first level is equivalence. Unlike identity that can be addressed on a yes or no basis, equivalence must be established within continuous ranges of variation. Thresholds beyond which variations are considered insignificant must therefore be defined, based on chosen criteria. In turn, the choice of criteria needs to be justified by clarifying the values on which they are based. The second level is comparison. This corresponds to the main issue addressed both in official documents of expert committees and in scientific reviews about SE. The toolbox for comparison discussed by expert committees involves as mentioned above: the choice of the comparators, trial protocols, list of compounds analysed, analytical techniques and statistical methods of analysis. The third level, the most obvious yet the least explicit, corresponds to substance, i.e. the object of comparison. Yet, no explicit definition of substance can be found in the OECD reports. However, the description of the comparison toolbox implies that the definition is implicitly restricted to end products. The context in which the food substance is produced is thus assumed to be irrelevant for its evaluation.
The exclusion from consideration of the context and the process of production has gradually increased in society due to the growing cultural prevalence of the assumptions of modern science, especially in the last two centuries. According to modern science, substance is the only valid basis for objective investigation. Therefore, SE *is* equivalence and, indeed, has been referred to as equivalence in some documents. A second aspect is that organic substance is assumed to be ruled by the laws of physics in the same way as inorganic, mineral substance. Therefore, the same procedures are used for both, based on analytical, quantitative methods. SE is not only a safety assessment tool as intended but it also provides a cultural picture of how our relationship to food is currently understood. In this picture, food appears as a context-free, quantitative aggregate of basic chemical substances. As a consequence, the main axis of improvement of SE is currently focused on the systematic detection of the largest number of compounds possible through the development of 'omics' profiling techniques.

3. The other legitimate factors and democratic implications

Scientific criteria based on objectification and quantification have been widely empowered in society and have acquired recognised authority for legal decisions. Science and polity have thus become closely intertwined and the resulting situation is called the 'Public Instruction Model' by the French sociologist Michel Callon (1998). In this model, modern science is the only core of knowledge officially recognised and endowed with legitimacy. In contrast, society is considered to be mostly ignorant and prejudiced and factors other than scientific, i.e. subjective factors, are either ignored or processed through objectification. As a result, the other factors have been reduced to 'risks'. Because risks can be addressed scientifically, the non-scientific factors can be rescued by the science-polity sphere of decision. As a consequence, the relationship between individuals and food substance has been mostly restricted to a risk quantification issue.
In the Public Instruction Model, the legitimacy of other factors and cores of knowledge besides science is mostly denied. The term 'other legitimate factors', i.e. other than scientific, can be found in the Agreement on technical barriers to trade of WTO (World Trade Organisation) documents. Also called 'WTO listed objectives', the other legitimate or authorised factors are as follows: national security requirement; prevention of deceptive practices; protection of human health or safety; protection of animal and plant life or health; and protection of environment. A main feature of these factors is that they are amenable to quantification, at least to some degree, and thus can be re-introduced into the scientific sphere. However, the 'other' other legitimate factors, including social, cultural, and ethical issues are not yet acknowledged in this picture.
Ethical values are addressed most of the time through consequentialist cost/benefit analyses. Benefits are considered to be regulated by the market through adjustment between supply and demand. But markets only have a weak ability to absorb risks, especially systemic risks associated with globalisation. Risks thus fall to institutions and this explains the prevalence of the risk discourse at the political level. In this context, only economic and political issues are acknowledged. The cultural, deontological dimension of ethics is mostly ignored if not denied.

However, background values and principles represent a large proportion of the other legitimate factors. As regards living organisms, these include among other values: intrinsic value and integrity; communality; autonomy and sustainability...
In our society, dominated as it is by the Public Instruction Model, ethics is to a large extent implemented through ethics committees. Like scientific expert circles, these committees operate as advisory circles for the politics. The idea of ethics committees implies that some form of knowledge and expertise is required to attain a qualified moral judgement and justifies that the deliberation about the common good is taken away from society. Since objectification is the basis of modern qualified cores of knowledge, subjective factors, hence background individual representations, tend to be ignored and eliminated from ethical deliberations. In the same way as the other subjective factors are reduced to risks, ethical considerations are thus essentially confined to objectifiable consequences, leading ethics committees into consequentialist rather than deontological reflection. The consequential dimension, including for instance the precaution principle, is further emphasised by the implicit political mandate of ethics committees. Paradoxically, ethics has thus become a means of maintaining a whole structure of institutions which is unable to acknowledge the cultural dimension in society.
The emergence of social controversy about food issues such as GMOs has raised increasing social demand for public deliberation. The Public Instruction Model is clearly not sufficient anymore and however enduring it may be, various dialogical models have already emerged to help incorporate the other legitimate factors and cores of knowledge in the deliberations (Callon, 1998; 2001). In this context, SE clearly appears as a cultural product of the Public Instruction Model. Scrutinising the controversy about SE leads to more profound democratic issues. The questions at stake are ultimately: who decides which criteria are relevant for food evaluation and on which values are they based?

4. A value-based equivalence approach: qualitative equivalence and ethical equivalence

To address the other legitimate factors, it is necessary to take into account the context in which food substance is produced instead of merely its composition and possible toxicological effects. To integrate the context of food production, the interaction between individuals and food substance can be divided into direct effects and indirect effects (Fig. 1). The direct effects correspond to personal interactions that occur when the food substance is actually taken in. The indirect effects correspond to interactions mediated *via* society even when the food substance is not taken in, for example pollution or unemployment. The sphere of direct interactions can be described by quality whilst the sphere of indirect interactions relates to ethics. The two spheres overlap to some extent and quality may be considered as one aspect of ethics.
Instead of rejecting SE, this concept may be complemented by two other equivalence concepts: QE, which relates to quality, and EE, which relates to ethics (Pouteau, 2000; Pouteau; 2002). The three equivalence levels together constitute an equivalence scale and only by considering these three levels can equivalence *per se* be addressed (Fig. 2). This equivalence scale can also do justice to food substance integrity. Food substance is not merely chemistry but it also embodies the context in which it is produced. Therefore, food substance integrity can only be respected by integrating the other legitimate factors, i.e. the context, in the evaluation process.
The context of the food substance includes three levels. The first level is the living organism from which the food substance is derived. The second level is the environment in which the organism develops, including the farming system, soil, water, air, etc. The third level is society which shapes the environment through human activities that are economical, cultural, and political. The three levels are integrated and embodied in food, as indicated by the arrowheads pointing inward on the diagram. This results in quality and can be assessed by QE (Fig. 3). But what methods do we have for the assessment of quality? If we resort to analytical and quantitative methods, quality will remain mostly confined to chemistry. It can be proposed that methods for the assessment of quality should be based on qualitative principles. These principles involve sensorial and aesthetic perception. The traditional methods used in sensorial laboratories, for example wine tasting, are

mostly based on sense perception. However, because of the growing concern of society for quality it is crucial to develop more methods and new approaches. One possible direction may be the use of aesthetic perception as in picture forming methods, for example sensitive crystallisation.
The QE concept can help to reveal how the context is integrated into food substance and is reflected by quality and allows the recognition of food substance integrity. Quality then reflects back on the context, as shown by the arrowheads pointing outward on the diagram, and reveals the ethical values at work at the different levels, organism, environment, and society. Ethical principles corresponding to the different levels can be tentatively proposed to identify the different dimensions of EE and provide a framework for an ethical assessment of food substance (Fig. 4).
The principle of dignity applied to the organism level was inspired by the reference to the 'dignity of creatures' (Würde der Kreatur) mentioned in the Swiss constitution and discussed in the *If*gene workshop in 2001 (Schmidt, 2001). However, referring to Kant, one may argue that dignity can only apply to human beings but not to plants or animals. Dignity may thus be replaced by the terms 'integrity' and 'intrinsic value', as proposed in this workshop. The four other principles are based on the French republican principles: 'Liberty, Equality, Fraternity' or 'Freedom, Equality, Solidarity' to which was added the principle of sustainability (Pouteau, 2000; Pouteau; 2002).
Sustainability applies to the environment level and relates to the protection and maintenance of natural resources. It involves a natural contract with living organisms and introduces a transgenerational dimension. The three other principles relate to the society levels. Solidarity corresponds to the sphere of interdependency and exchange, thus to economy. Freedom applies to the sphere of self expression and self determination, thus to the cultural sphere, including education, science, art, religion, tradition, etc. Finally, equality refers to justice, thus to the political sphere. As such, the equality principle is a transverse principle and it applies to all levels to guarantee transparency and loyalty.
The next question is: do we have tools for the assessment of ethical values? So far, there have been a number of endeavours in this direction, yet quite heterogeneous with regard to their content and operation. A growing number of companies and corporations have set up their own company code of ethical practice on a more or less individual basis. At a more collective level, frameworks and standards have started to emerge in the last few years to make ethical values operational in the corporate sector. For the sake of coherence and transparency, an Ethical Assurance could be set up besides the currently widespread Quality Assurance. The equivalence scale, especially the EE scale, may be instrumental in designing standards adapted to ethical values and to their respective sphere of application, so that the corporate sector can subscribe to part or all of the Ethical Assurance. The setting-up of an Ethical Assurance is highly dependent on the recognition of the other legitimate factors and the various cores of knowledge besides science. It needs to be established through a collective, transdisciplinary deliberation between the different actors of society in order to identify common ethical references.

5. Conclusion and discussion

The scientific controversy about SE does not reach nor even question the background assumptions on which this concept is based. The first session of this discussion was aimed at showing that the controversy is eventually not scientific but cultural. Analysing SE as a cultural product rather than a scientific tool can be instrumental in understanding the values underlying current food evaluation. This raises the issue as to what the legitimate factors for defining food should be and ultimately as to how food can be comprehensively defined. During the discussion, it was stressed that the labelling of most food products in terms of fat, protein, carbohydrate, and calorie contents had only emerged during the last two decades whilst information on food origin and process has made very little progress. This was compared to the reduction of complex medicinal compounds found in nature into purified active products. A reductive view of both food and remedies as aggregates of independent compounds having specific properties has inspired the idea that basic chemicals can be artificially synthesised and assembled to produce new products, such as GMOs, functional foods, and drugs. Another point of discussion was the question of the commercial double bind of SE with

regard to novelty and familiarity. Whereas GMOs are claimed to be radically new at a technological level, they must be presented as merely novel to the consumer for the sake of acceptability. By focusing on similarities rather than differences, SE seems specifically designed to emphasise the familiarity aspect of GMOs rather than their radical novelty. On the contrary, the procedure for listing new varieties in seed catalogues imposes the demonstration of a substantial difference so that the emphasis must also be placed on the radical novelty of GMOs.
To integrate values in the definition of food and address the issue of food substance integrity, additional equivalence concepts are needed. The objective of the second session was to show that a global assessment of food leads to wider democratic issues and the need to re-assess legitimacy by re-balancing economic and political issues with cultural values. This pointed to the necessity to implement qualitative and ethical assessments of food. During the discussion, it was concluded that although GM corn containing the Bt toxin was found SE, it would probably not pass QE and SE assessments. It was added that if a GM food is found SE, 'something else' must be different at least to justify patenting and commercial benefits. The term 'cosmetic biotechnology' was quoted to define this 'something' else'. The cosmetic aspect can only be revealed by addressing arguments such as ethical issues which have been ignored so far. Another point of discussion was the choice of the equivalence concept to address quality and ethics. It was argued that this term seemed already fallacious in the case of SE and that it should be abandoned in favour of another term, possibly simply 'assessment'. Indeed, equivalence imposes a comparison with something else and thus introduces the need to choose a reference and establish standards. The normative dimension of equivalence could lead to the imposition of a uniform view of what food ought to be. Yet, it was also argued that any assessment will introduce some form of comparison with something else and that changing the word might not solve the normative question introduced by evaluation procedures.

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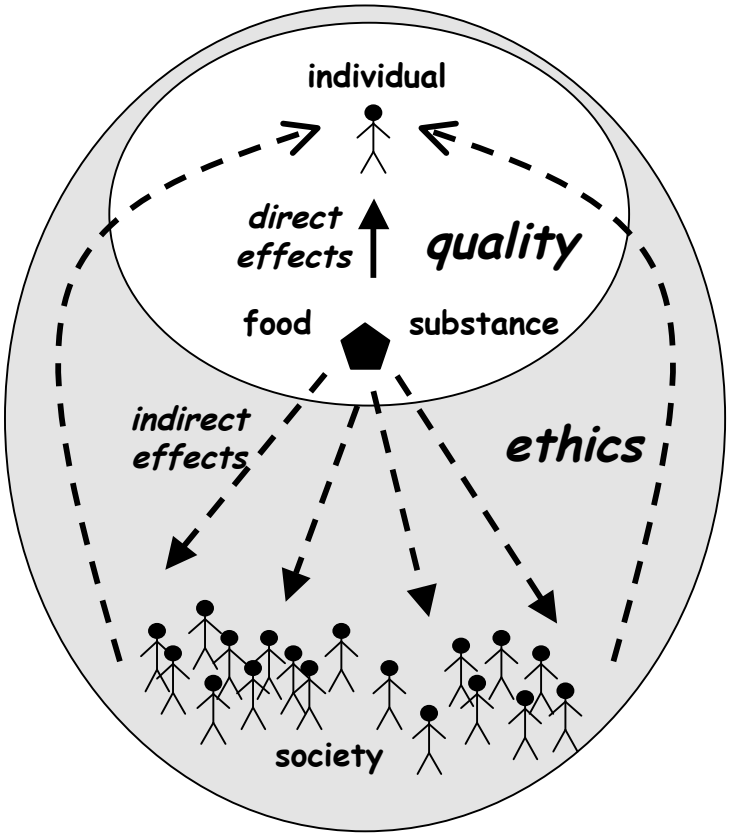

Figure 1 - Pouteau S 2002

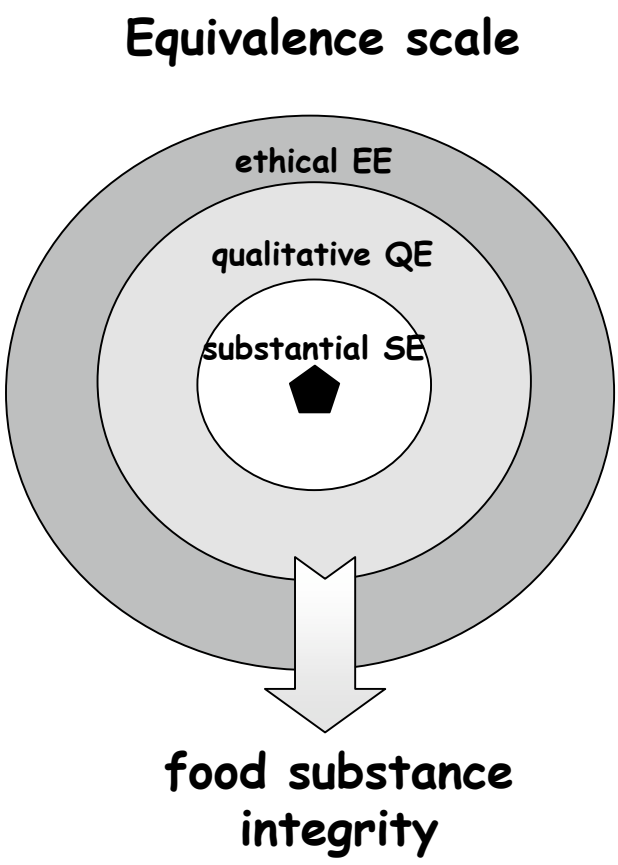

Figure 2 - Pouteau S 2002

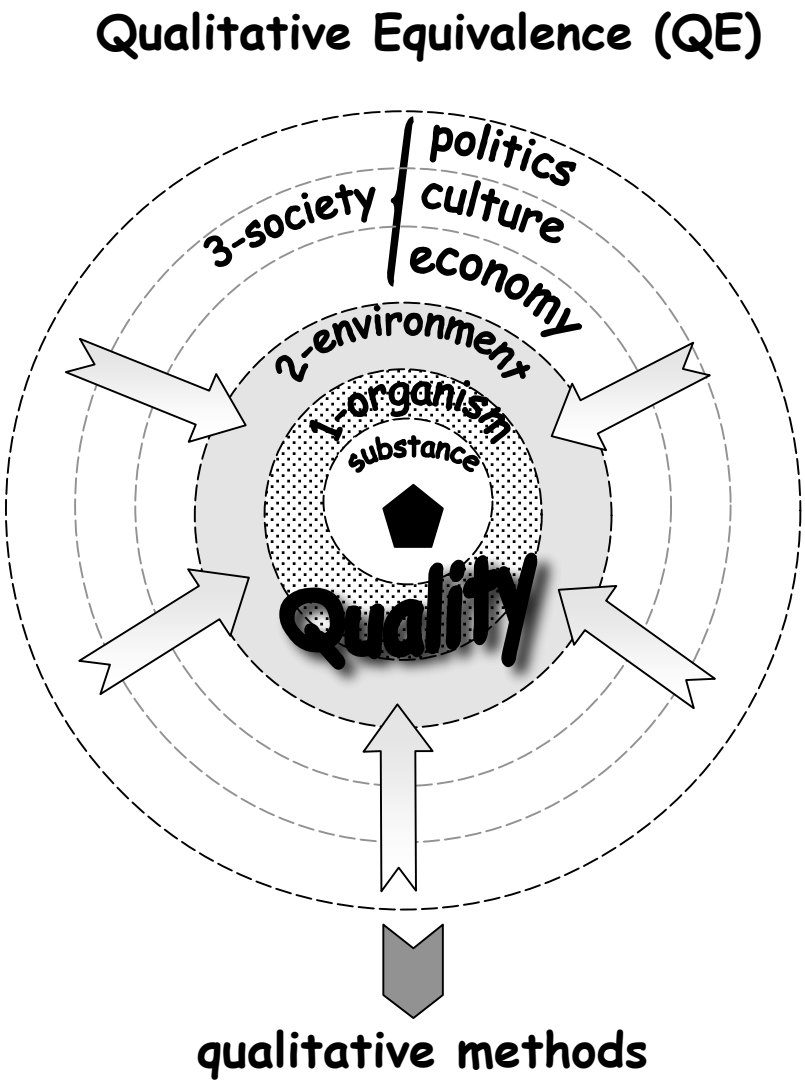

Figure 3 - Pouteau S 2002

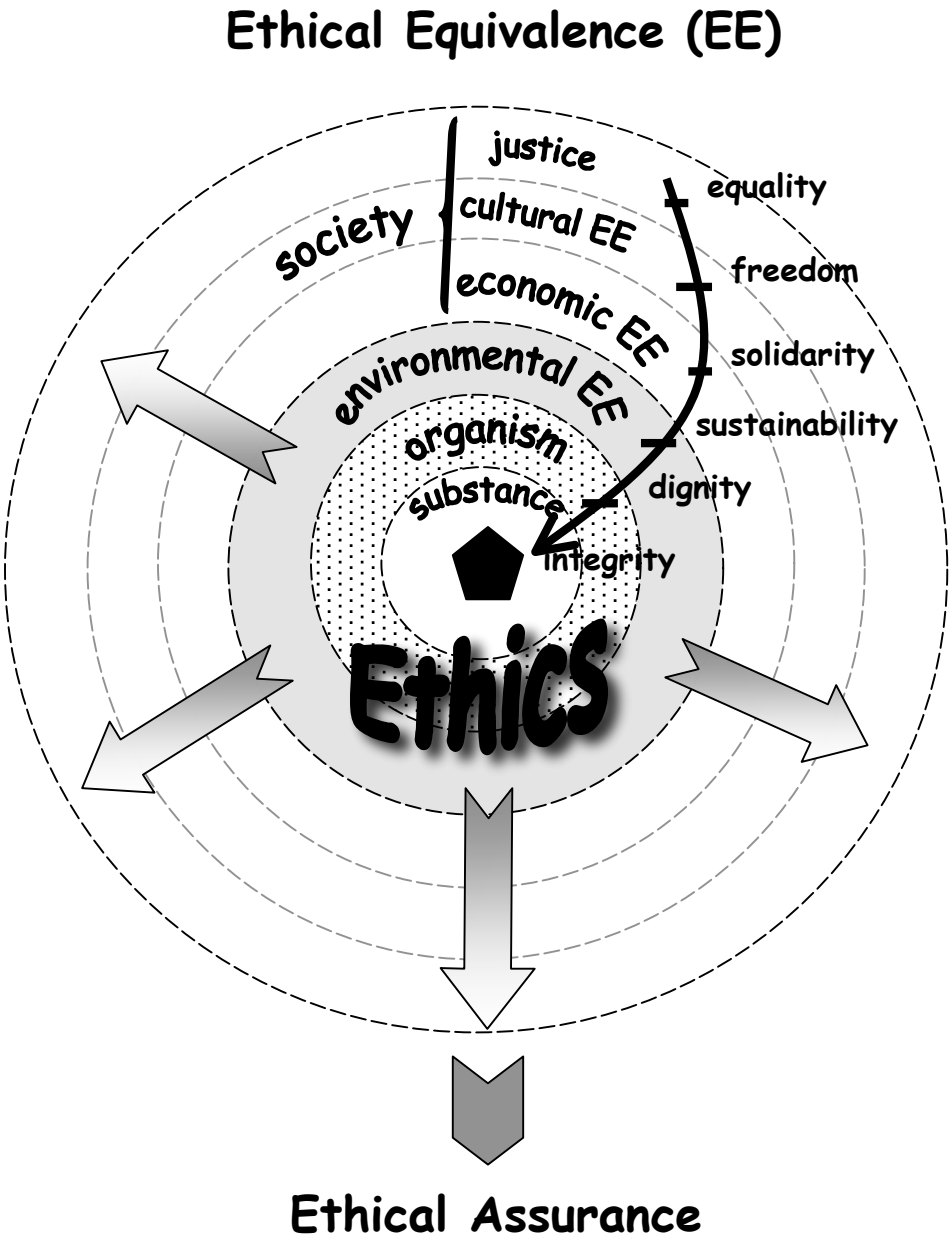

Figure 4 - Pouteau S 2002