Joint Advice Note issued by the French national Academies of Agriculture, Medicine, Pharmacy, Sciences, Technologies and Veterinary sciences in regard to a recent publication by G.E. Séralini *et al* . on the toxicity of a GMO

The French national Academies of Agriculture, Medicine, Pharmacy, Sciences, Technologies and Veterinary sciences, were acquainted at the same time as the general public with the paper published recently in the scientific journal *Food and Chemical Toxicology* by Gilles-Eric Séralini *et al*. where the authors claim that there is a strong tumorigenic and toxic effect in rats through consumption of genetically modified NK603 maize or through low level exposure to the weed-killer Roundup® to which the maize has become tolerant.

Faced with the widespread media mobilisation and given the impact on the public at large on this subject, the Academies have decided to issue a joint advice note covering various scientific, societal or deontological aspects of concern, and make a certain number of recommendations.

The Academies, however, decided that was no need to organize an in-depth expertise - among their Members, of the paper published by G.E.Séralini *et al.* - since this action has been entrusted to various specialised agencies and institutions who dispose of the expertise required. Two non-French agencies (in Germany and Australia/New Zealand) have already published their comments, as has the ESFSA[1] (European Food Safety Authority); all of these bodies refute the interpretations made of the results reported which they deem doubtful *per se*. France will soon be publishing the analyses of its National Food Security, Environment and Work Agency (ANSES) and that of the HCB (High Council for Biotechnologies).

Before we read these forthcoming advice notes, it is with their experience in research matters that the Academies signatory to this Advice note immediately challenge various scientific and deontological aspects of the G.E.Séralini *et al*. paper.

1° - Scientific considerations

The Academies signatory wish to draw attention to several serious shortfalls of the G.E.Séralini *et al.* paper.

Statistics and methodology

Toxicological experiments require testing a number of animals in adequation with the objectives, in order to ascertain an interpretable statistical value. In the case of the G.E.Séralini studies, lasting 2 years, a much higher number of animals would have been necessary, as is recommended in protocol

[1] *Cf.* http://www.efsa.europa.eu/fr/efsajournal/pub/2910.htm

guide-books, or, were the number used be lower, to only take into consideration a small number of groups that complied with certain precise criteria. Testing 10 groups each with 10 animals, only one of which was the control group, was a bad experimental option.

The 3 main questions addressed by G.E.Séralini *et al.* were: 1°) Could the GMO studied have either a toxic or a tumorigenic effect when absorbed alone? 2°) Could the Roundup® product studied, taken alone, have either a toxic or a tumorigenic effect? 3° Is there a specific associative effect through absorbing both products? The question of the GMO effects and that of weed-killer effects are completely separated, since biologically the two products have no comparison. This is important inasmuch as the media campaign was totally focused on the GMO aspects. To seek answers to his three questions, the experimenter would have been better advised to constitute 4 groups with a large number of animals: GMO alone, Roundup® alone, GMO plus Roundup together and a control group. The fact that G.E.Séralini *et al.* constituted 10 small groups does not allow one to discover answers to the questions. Indeed, classic statistical analysis of the results, such as presented in the authors' paper shows that there is no significant difference among groups, or, to frame it differently, there is no proven higher mortality nor tumorigenic effect by absorption of the GM maize, nor again of Roundup®, nor finally in an associative absorption of both GM and weed-killer, contrary to what the authors presented to the public at large. The assertion the authors made: that the animals fed with the GM maize presented more tumours that rats fed with conventional maize has no statistical founding. This result alone should have suspended the review phase of the paper, given that no toxicity effect whatever can be established.

Tumorigenesis

The Academies note that neither term "cancer" or "carcinogenesis" appear in the G.E.Séralini paper, nor indeed are these terms used in the article published in the magazine *Nouvel Observateur*; the term "tumour" which was used, is a source of confusion, given that everyone reads this as being equivalent to cancer and indeed this is the word that the media vehicled. The analysis given of life-expectancy rather that of mortality rate is unsatisfactory for reasons that derive from statistical methodology. Inferring that any death beyond the average survival life-span is a death due to "natural causes" simply cannot be accepted.

As far as tumorigenisis is concerned, the choice made by the authors to experiment with the Sprague-Dawley strain of rats is especially unfortunate. This strain spontaneously shows, on one hand, a high occurrence rate of tumours, demonstrating that it is genetically predisposed to developing tumours and, on the other, that any statistical analysis must consequently be carried out with a far higher number of rats (which was not the case for the G.E.Séralini experiments).

We can note here that the carcinogenic effects of glyphosate, the active ingredient (AI) in Roundup® have already been analysed in numerous publications not cited by the authors.

Other considerations

Several other misgivings can be raised:

- The animal food-stuff composition, *viz.,* the relative quantity of GM maize and Roundup® as well as possible presence of contaminants (pesticide residues, adjuvants, mycotoxins, *etc*.) is not detailed.
- No results are given for the relationship dose/observed effects, admittedly possible but unusual in toxicological studies. The presentation made by the authors of their methodology and results is very succinct whereas they had considerable scope to give the details in the Appendix that is posted on the journal's web-site (*op. cit.*). This procedure would have been especially welcome and justified given the media exposure that followed publication. Absence of details makes it impossible – for lack of complementary information – to implement studies aimed at reproducing the results announced here.

2° - <u>Societal consequences of the publication</u>

Orchestrating a scientist's notoriety or that of a research team constitutes, in itself, a serious demeanour when it contributes to generating and spreading fears in the general public that have no established or verifiable base. Research scientists must see themselves in the role of "watch-dogs", with the proviso that the hypotheses made, in the absence of validated, confirmed results, should not be presented or even perceived as possible proofs*, i.e.,* they warrant an application of the precautionary principle. It is therefore primordial that research scientists pay close attention to possibly serious consequences of any excessive assertions/statements they make.

To the extent that the 'consumers' do not have access to an adequate source/quantity of valid information, their fear of GMOs is reinforced, all the more so when "catastrophe-prone" press organs propagate the 'bad' news. This is a particularly serious state of affairs for those populations who consume large quantities of GM food-stuffs, such as is the case for South Africa. It is also deleterious for other countries where both planting/consuming of GMOs and research into GMOs can be inappropriately challenged.

3° - <u>Deontological and ethical considerations</u>

A intelligently orchestrated media mobilisation about research results that offer no valid conclusions raises a dual major ethical problem: 1° that of a team of authors who saw fit to organize a vast 'comm./media' campaign about their work, to an extent that the operation seemed motivated more by ideology than by the quality or the relevance of the experimental data, and 2° that of the review (*op.cit*.) that accepted to publish data which appear decidedly fragile from a series of points of view, not least of which is that of statistics.

Over and above our critical assessment of the actual contents of the paper, the way in which the communication aspects were managed also raises numerous questions, notably through the concomitant publishing of two books, the screening of a film and publication of a scientific paper the contents of which were all exclusive property of a single weekly publication, with a black-out embargo clause (that included the scientific community) till the date of the press conference. These conditions of circulating the paper and/or its contents, *etc*., to the press, who therefore were faced with an *a priori* impossibility to cross-check the findings and consequently unable to comment in good faith on the text and its conclusions, are simply unethical. The largely broadcast documentary film which followed and reported on the toxicological study as if the conclusions had been drawn in advance, and the publication of books by one of the authors, are both highly questionable attitudes.

The paper proposed by G.E. Séralini *et al.* was duly received by the journal April 11, 2012 (and accepted, August 2, 2012). Given the time-scale needed for the authors to finalise their draft paper, we can well assume that G.E.Séralini was in possession of all the data and results of his investigations, at latest by end-February 2012 and indeed by end 2011 had gathered sufficient data to conclude as he asserted, as to extreme "deleterious effects" of the GM NK603 maize and of the Roundup® ingested. If, furthermore, we assume that G.E.Séralini was convinced of the quality and relevance of his research work and the exactitude of his conclusions, the onus was on him to alert the highest sanitary authorities in France to draw their attention to the very serious threats that use of Roundup® and ingestion of the GM NK603 present to the populations concerned. These authorities would have rapidly commissioned an expertise report and gained valuable time, if deemed necessary, to implement measures to protect those populations. Holding back information - by the scientist G.E.Séralini *et al.* and by all those party to the results - is a serious professional fault.

In the process of communicating the results, the authors omitted to cite previous long-term investigations that led to publication of exactly opposite conclusions on the same topic; rigorous scientific research commands that there must be a discussion not only of the results obtained, but also citing the context of

all previous known results.

In regard to the "conflict of interests" that G.E.Séralini constantly opposes to other scientists, whatever their origins or specialist fields, we can also legitimately surmise if there are not any conflicts of interest for G.E.Séralini and members of his entourage, aware as we all are of their ecological stances and of the financial support they receive from major food distribution groups who base their advertising campaigns on the assertion of absence of GMOs in the food they sell to their customers.

4° - <u>Questions arising through the publication of the paper on-line in the scientific journal *Food and Chemical Toxicology*</u>

One of the tenets supposedly in favour of G.E.Séralini is the fact that his paper was published in an international scientific journal with a reading committee. Yet we all know that even the best journals, including the most prestigious, publish – fortunately in small numbers – papers that are mediocre in quality or occasionally turn out to be inexact in their conclusions. The journal in question, *Food and Chemical Toxicology*, has a satisfactory repute. The question therefore arises as to how a paper with such poor scientific value as that written by G.E.Séralini *et al.* was indeed accepted.

Consequently, the fact that the journal did accept is not a guarantee of the paper's scientific value, *i.e.,* the paper does not *per se* carry a label of quality. The shortcomings that were noted in the way the research work was conceived are so obvious that, indeed, we find it quite astonishing that the reading committee of a scientific journal of high repute accepted the draft for publication.

Whatever the circumstances, in science, publication is not alone sufficient to establish the proof of a purported scientific fact. It is through a conjugated and coherent effect of the scientific community, via the authors' peers, after publication, of independent validation of the results and their integration into a large corpus of data that allows the experiment(s) as reported to become scientific facts.

<u>Conclusions and Recommendations</u>

Thus it does appear, as per the arguments developed above, that the intense media and even political impacts set in motion by the divulgation of the G.E.Séralini *et al*. results were not at all based on evidence that went uncontested - as it should have been - given the consequences of the media treatment of the paper and its conclusions. Two clear responsibilities can be identified. Firstly, this scientific journal's editors, as said earlier, should never have accepted the paper for publication and this constitutes a serious matter inasmuch as expertise by scientific journals in general could be seen as replacing an initial peer-review assessment of the work. The second responsibility lies with the author G.E.Séralini who orchestrated in advance an over-blown media coverage using results open to refutation and without providing a start of a proof as to the veracity of his claims.

Having made these critical observations, however, it remains true that we have now undoubtedly reached an opportune moment to raise and examine the question of experimental protocols to be implemented to detect carcinogenic potential effects of food-stuffs. For instance, is the period of 3 months (the most commonly used time horizon) sufficient or not? This question is relevant probably for both pesticide and herbicide uses. But the problem is not as simple given that the time-scale, in particular as far as life expectancy is concerned, in rats or human beings. But it is certainly not this paper that should lead on to this sort of reflexion since it does not contain any proof as such. It would be especially dangerous even to evoke the possible need to conduct long-term experiments on the basis of this paper, insofar as it would give the impression that the results presented by G.E.Séralini *et al*. have sufficient validity to justify that the public at large suffers from a fear of GMOs, *etc.,* knowing full well the damage that such fears would cause both in France and round the world. A distinction must be drawn between assessing a sanitary risk when ingesting a food-stuff such as maize, from the assessment of a molecule or a product to which

humans can be exposed to low or very low doses, as in the case of glyphosates in Roundup®.

From a sanitary point of view, we must first of all reassure the populations and confirm the press releases already issued regarding the poor quality of this paper. The questions raised ought to be examined by well-recognized scientists who we can be assured have no conflict of interests, funded under a public control.

The media coverage of G.E.Séralini's paper and its impact on public opinion have been all then more impressive because this research touches on a topic, food safety issues, to which the French are highly sensitive. Television channels cycled the shock images that naturally struck the spectators' minds and thoughts. The channels thereby contributed to strengthen totally irrational fears to the extent that the results as presented (in the paper) carry no scientific validation.

For the purpose of limiting drifts of this nature, the 6 Academies recommend the creation of a High Committee for Science and Technology reporting to the Chairman of the French High Council for Audiovisual Affairs[2] whose remit would include alerting the Chairman about the way in which scientific facts approved by a very large majority of the international scientific communities are sometimes called to question in the media without the persons responsible for content of televised or broadcast information, for example, have verified the validity of the facts purported. Broadcasting or telecasting such "information" which may well be false will have had a deep-reaching negative impact on the French populations, altering their judgement. The High Committee proposed here would, in most cases, only be able to intervene *a posteriori* and hence should rapidly react to the extent that the issues and situations it would be called to assess would often call for rapid response.

[2] English rendering for the Haut Conseil de l'Audiovisuel – an advisory body created in 1972.