Remarks about the draft report of the « *High Level Expert Group on European Low Dose Risk Research* »

FUNDAMENTAL RESERVATIONS

Manifest smugness

Generally scientists aren't conceited about their possible « *High Level* ». However, maybe the name of the group is aimed to command non-scientists' admiration, what could be cleared up by considering the planned mailing list of the final report. As a consequence of such a surprising smugness, before looking at the text itself, a reader somewhat aware of the low dose risk concern will carefully look at the list of the group members in order to make up his mind about their real « level » in this domain.

Expert

According to the French AFNOR (Agence Française de NORmalisation) standard NFX 50-110, the « expert » is defined as a

« *Person whose* ***competence***, ***independence*** *and* ***integrity*** *earn him/her formal recognition as someone capable of conducting expertise work.* »

This implies what follows:
- **All the three** mentioned virtues are **required** to be recognised as an expert;
- When even only **one** of these virtues is **missing**, any formal recognition of expertise capability should be considered **null and void**;
- Due to the increasing numbers of scientific or hierarchical misconduct and of highly **overrated** reputations, the **only reliable** way to make sure that all of these virtues aren't lacking is asking real experts (meeting themselves the above definition) to **really** assess the **effectiveness** of each of them;
- « Independence » must be understood in its widest acceptation covering the present and past memberships, duties, responsibilities, beliefs... likely to generate all kinds of conflicts of interests:
    - o **psychological** (reputation, prestige attached to the duties...),
    - o financial (wages, allowances, fees...),
    - o personal (relatives, contacts...),
    - o professional (hierarchical or tutelary relationships, fulfilled mandates...),
    - o ...
- Usually, lacks of « Integrity » cannot be detected *a priori* and should, therefore, entail an *a posteriori* **eviction**.

Composition of the HLEG

The « *High Level* » epithet probably refers to the positions, duties, titles, bodies of appointment... of the members rather than to their personal competence in the « *Low Dose Risk* » domain: Jacques Repussard is the Directeur général of the Institut de Radioprotection et de Sûreté Nucléaire (IRSN), an institutional expertise body (the relevance of his contribution to the HLEG proposals depends on the information provided by his subordinates whose low dose risk assessments concerning the Chernobyl fallout in France and the radon have been openly seriously questioned); Elisabeth Cardis was formerly appointed to the International Agency for Research on Cancer (IARC), a branch of the World Heath Organisation (some of her colleagues didn't agreed with the methodology she used in one of her low dose effect studies). Some members of the group are obviously

not independent from previous **highly <u>questionable</u>** low dose risk assessments; it is therefore likely that their proposals might also be inadequate, what should have been avoided by setting a group of real « experts » (in the AFNOR sense).

Real motives of the HLEG

While **optimising** the strategic funding of low dose risk research is a very important and **necessary** issue, some of the specific goals presented in the draft report **<u>vindicate</u>** the scepticism bred by the group composition and plead in favour of an independent assessment of the report and of the contributions resulting from the consultation.

The first two paragraphs of the Executive summary set forth the pre-existing context of the HLEG formation. A well aware and attentive reader may notice a few **tendentious** writings and some **missing** others which do not match with the « apparently » balanced concern expressed in bold type letters and are out of place in the scientific community. This may result from a lack of competence in the low dose domain and/or from a **deliberate** intention to make a biased alarmist presentation of the possible related effects.

Making a start on peremptorily stating « *Both natural and man-made sources of ionising radiation [...]* ***<u>constitute</u>*** *a hazard for human health* » amounts to speaking of extremely rare situations and concealing the countless totally harmless ones!

Daring to write such a misleading cut and dried sentence suggests that the report might be **intended** for worrying and convincing **unaware** readers such as public sponsors.

Also the real motive of the HLEG setting-up should be clearly disclosed in the report: normally, initiatives for co-ordinating and optimising the European researches are incumbent upon the Research General Directorate of the European Commission or, in the particular field of the nuclear domain, upon the EURATOM. If the EC was informed and asked to appoint a representative **after** six key persons of five member states agreed in conceiving a research framework on low dose risk, the question is « who first had, and on behalf of what body, the idea of obtaining their consensus about such a project?

<u>TECHNICAL ISSUES</u>

Making clear a few points

It should be kept in mind that some of what is considered to be « ***known*** *about the quantitative effects of exposure to ionising radiation* » result from totally unacceptable and misleading studies; this contributes towards the remaining « *divergent views* ». The sentence « *The importance of low dose risk research is now recognised globally.* » calls for a few details: 1°) What kind of « *<u>importance</u>* » is it about? Improving basic scientific knowledge (such as understanding the *natural anticancer mechanism stimulated by extremely low doses of ionizing radiation* [Portess D. I. et al. (2007) Low-Dose Irradiation of Nontransformed Cells Stimulates the Selective Removal of Precancerous Cells via Intercellular Induction of Apoptosis. Cancer Res; 67: (3), 1246-1253])? Improving public or professional health protection against radiation? Arising or reassuring social fears? Perpetuating research funding?... 2°) Under what <u>threshold</u> a « *dose* » is considered to be « ***low*** »? Is it under the 95th percentile of the mankind natural exposure? Is it under the present lowest acceptable maximum exposure of workers? Is it under the maximum medical exposure of patients?... 3°) Under what threshold a « *risk* » is considered to be **<u>negligible</u>** (See [Duby J.-J. (1997) Risques réels et risques négligeables. Pour la Science; n° 241, p. 9])? Is this to be decided by researchers or by risk managers (politicians,

authorities, regulating bodies...)? 4°) **Who** « *recognised* » the « *importance of low dose risk research* »? The low dose risk researchers themselves (who are obviously non independent from the concern)? Real low dose risk experts meeting the above AFNOR definition (i.e. whose competence, independence and integrity have effectively been assessed and showed no deficiencies)?

Intended issues

Again, it is a pragmatic position not to consider « *the existing scientific knowledge* » as indubitable.

Some of the « *important issues* » presented arouse serious scepticism concerning the high level expert ability to propose realistic research programmes in the low dose risk domain:

« *the shape of dose-response for cancer* » may only be broached basically at the cellular or cultured tissue levels; **certainly not** through **epidemiological** studies. For mankind radiation protection, this kind of goal is fruitless given that any simple (e.g. linear no-threshold) or sophisticated (e.g. linear threshold, hypersensitive, logistic, hormetic...) model fitted upon effects observed for existing exposures should in no case be extrapolated to doses lower than **the one above which the predicted effect only starts to become statistically significant** given its uncertainty: first, starting from a very simple model able to provide a significant goodness of fit any additional sophistication should only be considered if it results in a significant increase of the goodness of fit (i.e. a **significant decrease** of the unexplained variability); second, it's unworthy to manage risks below the lowest significant one. The experts who proposed figure 2 on page 10 don't seem (or act as if they didn't seem) familiar with the proper use of models (See detailed commentaries below). Also the « *individual variability in cancer risk* » is fully **pointless** in a radiation protection scope.
« *tissue sensitivities for cancer induction* », « *the effects of radiation quality (type)* » and « *risks from internal radiation exposure* » are goals which reveal big **gaps** in the 1970s bibliography.

One may guess that the teams dealing with the « *risks of, and dose response relationships for, non-cancer diseases* » issue will do their best to **fabricate** more or less non-significant results which they will present as « **suggesting** » possible effects worthy to be studied in a sponsored larger scale!... As already stated on bottom of page 13, they will pretend that « *additional approaches are also needed* ».

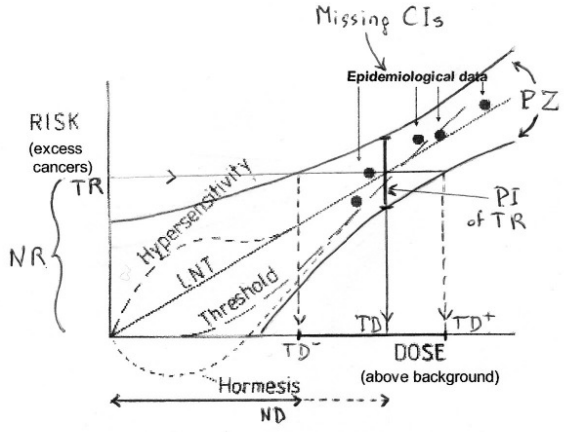
Epidemiologists should definitely learn that mentioning an inference whose significance level is clearly higher than 0.05 using terms which « suggest » that it might be true is **seriously unethical**: in 2004, Margot Tirmarche's team (IRSN) established a $p \approx 0.48$ world record (Jacques Repussard is well aware of the criticisms which have been expressed against several low dose risk assessments issued by his institute concerning the radon and Chernobyl fallout; Maybe he can't imagine that his subordinate advisers hide him the truth.) which has recently been beaten by a $p = 0.85$ value [Wilcox et al. (2008) Case-control study of radon and lung cancer in New Jersey. Radiation Protection Dosimetry; 128: 2, 169-179]! Would it be judicious to recommend them to play the Russian roulette with a revolver containing 48 or 85 live bullets in its 100 housings before writing down their conclusions?

Comments about figure 2

The high level experts who proposed figure 2 don't really grasp what a model is and what it can be used for. As mentioned in their legend, the figure represents possible « *dose-*

response relationships », i.e. relationships between an explanatory variable (the « dose ») and an explained variable (the « response »). Along the abscissas axis they kept « dose » as the name of the explanatory variable and along the ordinates axis they specified « risk » as the name of the explained variable what perfectly corresponds to the real (though more or less unknown) carcinogenic process. Unfortunately, in brackets, they changed these variable names into « dose above **background** » and « excess cancers » respectively: These changes present a serious inconvenience: 1°) The dose is a physical variable perfectly defined: even if the 0 Sv dose isn't encountered in our universe, it is a very good origin which makes any dose comparable in Briançon or in Montmorency with the same ability to explain the observed risk. 2°) The dose above the background depends upon what this arbitrary background is and has no more a physical existence, what reduces considerably its explanatory ability, particularly in the low-dose domain the experts are interested in: a same dose above the arbitrary background dose doesn't correspond to the same real dose and therefore can't be expected to induce the same excess cancers in Briançon and Montmorency.

The « *diagrammatic representation* » which is presented shows no confidence intervals (which are generally very wide) around the epidemiological data. In their publications, epidemiologists use to focus on the confidence interval of the sole slope of the model they have fitted; this is totally inadequate for radiation protection goals because they are not allowed to infer from an overall significant relationship observed in a given dose domain that the response predicted by their model is significantly higher than the maximum one which the risk manager considers to be negligible (what is incumbent on the regulatory authority to decide, not on so-called experts): in fact, they must provide the regulatory bodies with low-dose risk and attached uncertainty estimations and they must be able to estimate proper significance levels of comparisons between predicted or estimated risks or between an observed or predicted risk and a reference one. The figure 2 clearly shows that the available epidemiological data give no information at all about the shape of the dose-response relationship when the doses are below the observed domain: only very mediocre epidemiologists may hope or pretend that extrapolating their model to this domain will « create » information useful to the risk manager. However, should they know what a « prediction zone » is, they must inform him of the dose above which the response becomes significantly higher than the one which he considers negligible (and they should refrain from bothering him with wild imaginings of what lower doses might induce). This is illustrated by the following proposed completed figure 2 for the LNT case:



It's the regulatory authorities' responsibility to decide above which threshold response (TR) they intend to « manage » the risk and it's the statistician's duty to inform them whether or not this response is significantly higher than the proper reference population risk given its corresponding prediction standard error (used to estimate the prediction interval PI); if the difference isn't significant, he may suggest the authorities to adopt as a realistic TR the lowest response which shows a significant increase compared to the reference population risk and deduce from the model and its prediction zone (PZ) what the corresponding

threshold dose TD and its confidence limits TD^+ and TD^- are. All doses below TD are negligible doses ND which induce negligible responses NR.

Confounding factors

When a risk factor other than the studied possible ones is predominantly implicated in the studied effects it should not be considered as a simple « ***confounding*** *factor* »: epidemiologists are asked to 1°) first of all, take the **sole** predominating risk factor into account in their **reference** population in the same way they intend to take it into account in their studied population; 2°) given the uncertainty of its predicted effect in this reference population, deduce what the additional effect attributable to the studied possible risk factors must be to be significantly detectable and whether or not their studies are « feasible »; 3°) take the predominant risk factor into account in their studied cohorts **before** looking for a **possible** additional « significant » effect of the suspected risk factors; 4°) publish the significance level attached to the additional effect inference without any **captious** writings in case it is not significant.
Because smoking (which is involved in more than 95 % of the deaths from lung cancer in the general population) has only be taken into account as a confounding factor by summary corrective coefficients or rough categorical adjustments (« never/ever/former smoker »), **all** the radon studies which were presented as supporting its noxiousness are **unacceptable** (see [IARC (2007) Attributable causes of cancer in France in the year 2000. IARC working group reports: ISBN 978 92 832 2443 4] on page 123); unfortunately, they were the basis of the present **expensive wasteful** regulations which manage, in fact, a purely **speculative** risk. Badly managed trans-national cohort studies result in a seriously misleading overall conclusion: by now, the **only** way to detect a possible effect of radon is to consider **strictly** non-smoker cohorts (neither « active » **nor** « **passive** » smokers). It's particularly regrettable that expertise bodies **well aware** of the criticisms expressed against their low dose risks assessment methodology persist in ignoring them (while they seem, in private, to agree they are relevant) and continue to publish their rehashed same old refrain [Vacquier et al. (2008) Mortality risk in the French cohort of uranium miners: extended follow-up 1946-1999. Occup. Environ. Med.; 65: 597-604] (probably to protect their fame) rather than **confess the truth** to the Authorities who were **misled** by they previous unacceptable conclusions which are the basis of the present regulation.

While co-ordinating and optimising the European radiation protection research is a praiseworthy goal, given the above remarks, **the present draft report looks like a blurb aimed to justify the sponsoring of low dose research proposed by existing teams and presented by a so-called « high level » expert group** with the likely aim to convince some European national funding authorities. **It is obvious that many non-expert** (according to the AFNOR definition) **judge and judged people are involved in its writing. This draft report should be carefully assessed by real experts (upright, competent in all the broached domains and independent from all the represented bodies and HLEG members) before being released and a watchful quality assessment of the concerned teams and of the expected studies and results should be set up.**