

Minority Report on:

VPC REPORT “RISKS ASSOCIATED WITH THE USE OF HORMONAL SUBSTANCES IN FOOD-PRODUCING ANIMALS”

The VPC Report, recently approved by the VPC for submission to the Secretary of State, spells out the many uncertainties and grey areas that exist, as well as the incomplete science associated with hormone growth promoters.

The Working Group and the European Commission’s Scientific Committee on Veterinary matters relating to Public Health (SCVPH) are obviously in total accord when they state that there are important gaps in the evidence base that precludes producing a definitive risk assessment for five hormonally active substances, but is enough for a permanent ban for one of them (oestradiol 17 beta).

However, the Report is incomplete. Official reports, published papers and statements of other bodies have been omitted. Additionally, the VPC Summary of Responses to the consultation on the draft paper contained only a partial summary of, and comments on, selected items, and this will now form a supplement to the HGP Report.

I therefore wish to dissociate myself from this VPC Report for three reasons:

1. The decision of the Working Group as recorded in the Report (overview – Page 3), is that it was **unable** to support the conclusions reached by the SCVPH, namely that “the risks associated with the consumption of meat from hormone-treated cattle, may be greater than previously thought”.

With this part of the decision I cannot agree, since the latest evidence shows that many more potential risks have been identified since the first 1999 VPC HGP Sub- Group Report was published. Indeed, during our three-year period of examination (2002-2005), further scientific evidence which the VPC Report does not even examine, has revealed reasons for even greater concern.

2. The publication of the Report – plus a supplement – was not envisaged in May 2005, when we discussed the Draft Report at the VPC Meeting. The minutes of that meeting stated that “the working group would consider and present a revised report to the VPC for adoption as its final Report”. This should be done not with an attached supplement or an attachment which may or may not be read, but with a proper revision of the Report itself. As we are all well aware, because of the volume of literature to be read today, many people do not get beyond the executive summary abstract.
3. The working group has not met for fourteen months, although it was promised that outstanding matters of considerable importance could be discussed, along with other comments from the consultation responses.

I am obliged to issue this minority report because consideration has not been given to important papers which are clear evidence of the risk to human health posed by these hormones.

1. ***THE 10th and 11th US REPORT ON CARCINOGENS*** – by the National Toxicology Programme - classified for the first time in 2002 oestrogens as: “*known to be a carcinogen*”.

This means that there is sufficient evidence of carcinogenicity from studies in humans that oestradiol can both cause and promote human cancer. This is what the relevant scientific committee of the European Commission has also found.

These US Reports, in which the US Food and Drug Administration (FDA), the US Environmental Protection Agency (EPA), the US Occupational Health and Safety Administration (OSHA) and the US Product Safety Commission (PSC) participated, also stated that:

“veterinary use of steroidal estrogens (to promote growth and treat illness) can increase estrogen in tissues of food-producing animals to above their normal levels”.

These reports on carcinogenicity are evidence of the risk to human health - when the VPC Report (page 4 item 5) refers to “the current lack of evidence of a risk to humans”.

As oestradiol has been pronounced carcinogenic and as the VPC Report also states that “it would be prudent to consider Oestradiol and its metabolites as a carcinogen, whilst more substantial evidence for its mode of action is obtained” (page 35, 10.1.7), one must question why this is not properly reflected in the Report. Instead, prominence has been given (in both Over-view page 3 and Conclusions and Recommendations page 4) to the “conclusion” that:

“the weight of evidence at present available suggests that the likely levels of human exposure to hormonally active substances in meat from treated animals, would not be sufficient to induce any measurable physiological effect”.

If oestradiol is carcinogenic, then such a statement seems not only illogical and scientifically unsound, but irrelevant.

US scientists who worked for, or are funded by the US Government, have consistently and increasingly over the years been arguing, that residues of these hormones in meat are carcinogenic, no matter how small are the levels. The argument that there are safe levels below which there is not risk, is now regarded as an out-dated argument.

Daniel Sheehan, another well known EPA scientist, has very recently published a paper arguing convincingly that there is no threshold dose-response for estrogens (see *Environmental Research*, 100 (2006) 93-99).

A further very recent comment from *Chemistry and Industry*, 6th February 2006, is also very relevant. It states “there is a growing crisis over which dose-response model should be used is a risk assessment in the field of toxicology. For decades government

John Verrall

risk assessment actions have used a threshold model to govern exposures to non-carcinogens, while a linear model has been used for chemical carcinogens. However, strong and, many would say, convincing evidence has shown that these very long-revered models are flawed where it counts most – in the low-dose zone.”

The Hormesis dose-response model, characterised by a low-dose stimulation and high-dose inhibition, is more common and fundamental than the models currently used, and should replace them in the risk assessment process.”

2. Recent Paper on *Transformation of MCF-10A Human Breast Epithelial Cells by Zeranone and Estradiol – 17b* (*The Breast Journal Volume 10, No6, 2004, 514-521*)

This Paper by Professor Young Lin and workers from Ohio State University demonstrates that meat and even serum from Zeranone-implanted cattle contains such high hormonal residues that they stimulate the growth of normal and cancerous breast cells in tissue culture.

The results of their work indicate that both Zeranone (a synthetic hormone growth promoter) as well as oestradiol can induce human breast epithelial cell neo-plastic transformation with similar potency. And they argue that:

“Zeranone (Ralgro) is a nonsteroidal agent with estrogenic activity that is used as a growth promoter in the U.S. beef and veal industry. Thus zeranone is not an environmental contaminant per se. Rather, people are exposed to zeranone as a result of introduction of the compound into food animals by veterinary professionals on behalf of beef industry farmers. We have shown that meat and serum from zeranone-implanted cattle possess heat-stable mitogenicity for cultured breast cells, and that both normal and cancerous human breast cells exhibit estrogenic responses to zeranone”.

The Ohio Paper is not included in the Report, nor in the supplement to the Report, neither are three other statements relating to Zeranone, which came to light in responses to the Draft Report. Statements by:

- The Committee on Mutagenicity that Zeralenone “should be considered as being potentially genotoxic *in-vivo*”;
- The Food Standards Agency: that “until a definitive statement of all scientific data on Zeranone and Zeralenone can be taken, a precautionary approach should be taken and both should be considered potentially genotoxic”.
- The Foods Standards Agency: “a ban on Zeranone would be prudent”.

The Conclusions and Recommendations on Zeranone in the Report (page 28) paradoxically state that: “the Working Group concluded that there are insufficient data to indicate that Zeranone and Trenbolone are genotoxic.” I think such a statement is scientifically at odds with the available evidence and difficult to justify.

John Verrall

3. ***Toxicological report on endocrine disruptors – low dose review 2001 (USEPA, NIEH, NIH)***

This report has confirmed the views of the SCVPH that there is no question of a threshold and that any endogenous hormonal substance or external endocrine disrupter is of significance, and cannot be discounted in any way.

The VPC Working Group maintain that because oestradiol shows negative to the Ames Test, it cannot be genotoxic. The relevant scientific committee of the European Commission maintains that oestradiol is not the only established carcinogenic substance that does not show positive in an established mutagenicity test. So that it considers 17 beta oestradiol to be a complete carcinogen and to be both tumour initiating and tumour promoting, an opinion shared by a growing number of scientists.

4. **Some of the other matters that give rise to concern to me and which are not properly or not at all addressed by the Report:**

A - *The VPC consideration and comment on the responses included: “The VPC is unaware that there is growing evidence for the cocktail effect.”*

But the report (p.34 para 3) does acknowledge that: “We do not have enough information about their (synthetic hormones and lipoidal esters) interaction within natural hormones in humans”. However, synergism is apparent when trenbolone and estradiol are used in combination in veal calves (Gropp et al.) Environ. Qual. Saf. Suppl. p.131 – 141).

Also “Weak Estrogenic Chemicals Combined at Concentrations below NOEL’s Produce Significant Mixture Effects”, the authors of which paper (Environ. Sci. Technolo. 2002 p.1751-1756) conclude that: “Hazard assessments that ignore the possibility of joint action of oestrogenic chemicals will almost certainly lead to an under-estimation of risk.” This is of course particularly true when risk assessment is not comprehensive and where there is no dialogue between risk assessors and risk managers.

B - *IARC statistics*

The two principal causes of cancer in men and women are prostate and breast cancer respectively. If IARC statistics are examined – for 1997 (the only ones available to me) and you compare the incidence of these cancers in white US women and men and European women and men (chosen thus, as far as possible to eliminate genetic difference) these are as below:

	<u>Breast Cancer</u>	<u>Prostate Cancer</u>
White US women/men per 100,000	97	96
European women/men per 100,000	67	37

In the Ohio Paper by Lin et al. mentioned above, they point out that white US women have a five-fold greater risk for human breast cancer than Asian women in China and Japan. Furthermore, they point out that the risk of acquiring breast cancer among Asian women immigrants in the US approaches that of American women after one to two generations. Apart from these very significant and specific variations, however, what is very evident is the fact that US women and men experience about 20-25% higher rates of cancer than women and men in Europe, where hormone-treated meat is not allowed since 1982.

John Verrall

These observations must indicate strong influence from a number of external factors, such as diet or environmental, rather than genetic component in the aetiology of this disease. It has been speculated that dietary factors may contribute to this ethnic difference in human breast cancer incidence. Lower urinary levels of oestradiol oestrone and oestriol are excreted by Singapore-Chinese women than US women (Urisin et al, 2001), and this must support a positive association between breast cancer incidence and oestrogen exposure.

These interesting figures in fact prove nothing, but do serve to emphasise the need for caution and the need to establish criteria and make decisions based on science – and not the absence of science. Both the SCVPH and the VPC are in total accord when they state that there are important gaps in the evidence based that preclude producing a definitive risk assessment.

The British Veterinary Association (in their response to the Report) were unclear “whether the VPC is attempting to make a case for the re-introduction of these products or highlight the need for further research,” however they obviously perceived the uncertainties and possible consequences when they stated: “Given these uncertainties, the European ban seems the safer route to follow, particularly as there is no need, other than economic gain, to use these hormones”.

C - Other statements on food safety and environmental issues

The Foods Standards Agency confirmed that:

“Should there be any move to change the current ban on hormone growth promoters, that they would want a thorough review of the food safety issues”, and with this the VPC agreed at their meeting (see VPC Minutes May 2005).

However, this statement is not included in the VPC report nor in the supplement. This statement should be included together with the statement on environmental issues, namely that:

“It is assumed that if the re-introduction of growth promoting substances for use within the EU were considered in the future, then a full environmental risk assessment would need to be conducted according to good current scientific practice.”

Although featured in the body of the report (Page 33, Para 7), both statements should in my view have featured prominently in the summary of the Report’s Conclusions and Recommendations.

Additionally, the Report does not contain any consideration of Animal Health and Welfare. However, in the Summary of Responses, it was stated that: “The EU would need to look closely at any adverse affect on animal health and welfare.”

It should be remembered that, besides the concern for human health, it was the established severe adverse affects on animal health and welfare, which was a principle reason for banning the use of another kind of hormone (bovine somatotropin).