United States – Continued Suspension of Obligations in the
EC – Hormones Dispute

(WT/DS320)

Second Written Submission
by the European Communities

Geneva
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INTRODUCTION

1. In this Second Written Submission the European Communities will address the specific arguments presented by United States in its First Written Submission, its Oral Statement and its Replies to the Panel’s and EC questions. The European Communities will refrain from repeating in full its claims and arguments set out thus far. These claims and arguments are still valid and are complement by this submission.

2. At the outset, it is worth highlighting the main contradictions and confusions as they result from the United States written and oral submissions thus far:

   ➢ The United States argues that the continued suspension of concessions is not intended to “seek redress of a violation” within the meaning of Article 23.1 of the DSU because of the existence of the DSB authorization. However, the United States cannot give a meaningful answer regarding the purpose of the continued application of sanctions since the basis of the DSB authorization, i.e. the original EC measure, has been removed. Either it seeks redress of a violation resulting from the inconsistency of the old measure or of a violation resulting from the inconsistency of a new measure. In the former case, there is a violation of Article 22.8, in the latter of Article 23.

   ➢ The United States argues that it has not made a “determination” about the alleged WTO-inconsistency of the EC implementing measure. However, this argument is in obvious contradiction to what it has repeatedly stated in the WTO and other public fora. This argument is also inconsistent with the very fact that the United States continues to apply sanctions against the European Communities.

   ➢ The United States even pretends that there is no “disagreement” with the European Communities as to the WTO-consistency of the EC compliance measure. This statement is impossible to reconcile with the United States’ repeated criticism of the EC implementing measure and its continued application of sanctions.
The United States confuses the concept of a “termination” of the DSB authorization and that of its continued “application” by the suspension of concessions and related obligations. For the purposes of this proceeding it is not necessary to contemplate when and under which conditions the DSB authorization could be “terminated”. All that needs to be decided in this dispute is whether the application of the suspension of concessions may continue in circumstances such as those at hand. The question regarding the “application” of the DSB authorization by the suspension of concessions and related obligations is obviously different from the question about the existence or “revocation” of the DSB authorization. While the latter is not expressly regulated in the DSU, the former is.

The United States finally denies that the principle of good faith is of general relevance to the WTO agreements. The United States’ argument is thereby not only in stark contradiction with constant WTO jurisprudence, it also puts into question the very foundations of the WTO agreements.

3. The EC case is straightforward: WTO Members that apply sanctions against another WTO Member cannot simply adopt a lean-back-and-wait-attitude over years and continue to suspend concessions in the presence of a subsequent compliance measure. Just as WTO Members who have been found to be in violation of the covered agreements have an positive obligation to implement, so have retaliating Members an positive obligation under Article 22.8 of the DSU not to apply sanctions any more and/or, if they disagree with the compliance measure, to initiate WTO proceedings under Article 21.5 of the DSU. This has always been the practice in WTO proceedings. If a retaliating WTO Member fails to respect these rules and procedures under the DSU it will be in violation of Articles 23.1 and 23.2(a) of the DSU. Conversely, the politically more convenient attitude to continue to apply sanctions as if nothing has happened is not an option under WTO law. Indeed, it contradicts the very purpose of the DSU.

4. In the following sections, the European Communities will address in more detail a number of arguments made by the United States. It will also take this
opportunity to rebut the United States’ claims regarding the WTO-inconsistency of the EC implementing measure. These rebuttal arguments are notwithstanding the European Communities’ repeated view that the Panel is not required to address the substance of the EC compliance measure in order to find a satisfactory solution to this dispute. However, as these arguments constitute the main defence by the United States the European Communities will address the issues in the second part of this submission.

**PART 1: Violation of Articles 23.1, 23.2(a), 21.5 and 22.8 of the DSU (systemic issues)**

I. **THE UNITED STATES IS IN VIOLATION OF ARTICLE 23.1 AND 23.2(A) READ TOGETHER WITH ARTICLE 21.5 OF THE DSU**

5. As the European Communities has argued in its First Written Submission, the continued application of sanctions by the United States despite the adoption of the EC compliance measure is in violation of Articles 23.1 and 23.2(a) in conjunction with Article 21.5 of the DSU. Under these provisions WTO Members are prohibited to seek redress of a violation on the basis of a unilateral determination that a violation has occurred. Instead, WTO members are required to have recourse to a compliance proceeding as provided under Article 21.5 of the DSU.

6. From the outset, the European Communities notes that the United States agrees with its interpretation of the relationship between Article 23.1 and Article 23.2(a), namely that whenever there is a violation of Article 23.2(a) there is also a violation of Article 23.1 of the DSU. However, where the European Communities and the United States disagree is whether the continued suspension of concessions is a form of “seeking redress of a violation” (Article 23.1 of the

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1 US Reply to Panel Question 44.
DSU) and whether the United States has made a “determination of inconsistency” (Article 23.2(a) of the DSU).

7. The European Communities will address both issues in turn.

(a) Article 23.1 “seeking redress”

8. The United States argues in essence that the continued suspension of concessions is not a form of “seeking redress” against an (alleged) WTO-inconsistency of the EC compliance measure because the sanctions are based on the DSB authorization and this authorization is unaffected by the European Communities’ “declaration” of compliance.2

9. However, as the European Communities has already explained, the existence of a DSB authorization does not exclude that a WTO Member is still seeking the redress of a violation within the meaning of Article 23.1 of the DSU. Indeed, the very fact of applying sanctions implies that a Member is seeking to redress a violation. Such an application of sanctions may be justified if a measure by a WTO-Member has been properly found to be WTO-inconsistent and, if on that basis, the DSB authorizes the suspension of concessions.

10. However, the situation is different regarding the continuation of sanctions in the presence of a compliance measure which the DSB has not found to be WTO-inconsistent. A DSB authorization which has been granted in view of an original WTO-inconsistent measure can not justify the continued application of sanctions against a different measure which has never been found multilaterally to constitute a WTO-violation.3 Rather, since the application of sanctions requires a causal relationship to a WTO-inconsistent measure it is clear that any present application of sanctions must be linked to a present measure. Conversely, it is logically not possible to justify the present application of sanctions to a past, no longer existing measure just as it would be impossible to link the present application of sanctions to a future, not yet existing measure. Thus, since the

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2 US First Written Submission, paras. 175 et seq., US Oral Statement, paras. 39 et seq.
3 EC Oral Statement, paras. 27 et seq.
sanctions are being applied every day, their continuation is a continuing act of “seeking redress”.

11. To accept the US argument would lead to the absurd result that the United States could continue to apply sanctions irrespective of any events occurring after the DSB authorization. For instance, even if the European Communities were to lift the import ban for hormones treated beef the United States could still apply sanctions since the DSB authorization still exists. Thus, in such a scenario, where the United States would consider the European Communities to be in compliance\(^4\), the United States would still assume a right to apply sanctions.

12. The US argument is also absurd in the light of the object and purpose of sanctions, i.e. to induce compliance and to rebalance rights and obligations in case of a WTO violation. If the United States apply sanctions merely because of the existence of a DSB authorization and irrespective of a subsequent compliance measure one may reasonably ask what are they currently inducing? And what are they currently rebalancing? The answer must necessarily be “nothing”.

13. In this context, the European Communities considers the US answer to Question 39 rather superficial. The United States argues that its sanctions are not in response to the EC compliance measure since the sanctions have never been altered. However, what the United States fails to acknowledge is that the situation has been altered by the adoption of the EC implementing measure. The United States is well aware of this change. And it has indeed taken a negative position on the EC compliance measure. Moreover, the United States has been under no obligation to continue the suspension of concessions. The very fact that it nevertheless does it in this new situation demonstrates that it indeed considers there is a causal link between the continuation of the suspension and the determination of inconsistency of the EC compliance measure.

14. In this context, the European Communities would also draw the Panel’s attention to the US First Written Submission where the United States explicitly states that it “is not seeking redress for anything but the import ban which the DSB ruled

\(^4\) See US Reply to Question 46, para. 16.
inconsistent with EC obligations (…)). If this statement were taken literally it would mean that the United States is currently applying sanctions against a no longer existing measure because the measure which the DSB ruled inconsistent has been removed by the EC compliance measure. However, if we consider more accurately that the United States continues to apply sanction because of the existence of an “import ban” as such it would do so against a new measure (since the current import ban is different from the one which the DSB found WTO inconsistent). Yet, this new measure has never been found WTO-inconsistent by the WTO.

15. From a legal policy point of view, there can equally be no doubt why the United States refuses to admit the obvious: Since the United States has once upon a time received a DSB authorization to apply sanctions it wants to keep full discretion on when and how to use it. Thus, even in the presence of a compliance measure the United States assumes a right to determine unilaterally whether this measure is sufficient or not. This, however, is not acceptable from the perspective of the multilateral trading system.

16. The United States’ argument that it is not seeking to redress a violation by the continued application of sanctions is also contradicted by its assessment of the EC compliance measure. The European Communities will address this in more detail when we discuss the term “determination” under Article 23.2(a) of the DSU. However, at this stage, it is already useful to recall the US statement in its 2005 Trade Policy Agenda:

The United States maintains its WTO-authorized sanctions on EU products because the United States fails to see how the revised EC measure could be considered to implement the recommendations and rulings of the DSB in this matter.

17. This statement speaks for itself. The United States thus openly links the continued application of sanctions to the EC compliance measure. Conversely, the United States did not state that it continues to apply sanctions because of the

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5 US First Written Submission, para. 176.
6 And this is what the United States has obviously in mind, see its Reply to Question 46, para. 16. The United States also admits that an import ban can be a different measure depending on the underlying risk assessment, US Reply to Question 54, para. 36.
DSB authorization. This statement also disproves the fallacy alleged by the United States about what is “after” and what is “because”.

For these reasons, the European Communities considers that there can be no doubt that the United States is currently continuing to apply sanctions because it seeks to redress an alleged (continued) violation by the EC compliance measure.

(b) **Article 23.2(a) “determination”**

19. Related to the meaning of “seeking redress” is the unilateral United States’ “determination” that a violation has occurred. The United States denies such a “determination” and it presents its objections to the EC compliance as mere “internal deliberations”. In its reply to the Panel Question 41, the United States furthermore tries to draw the “ironic” conclusion that the EC interpretation would convert this provision from a *prohibition* to make determinations into an *obligation* to make them.

20. The term “determination” is defined, *inter alia*, as an “authoritative opinion”; “a conclusion reached”; “the action of coming to a decision”; “the result of this”; “a fixed intention”. This term has been further elaborated by the Panel in *US – Section 301* whereby

   a determination implies a high degree of firmness or immutability, i.e. a more or less final decision by a member in respect of the WTO consistency of a measure taken by another Member.

21. In the same footnote the Panel continued that

   what is decisive under Article 23.2(a) is not so much whether an act constitutes a “determination” – *in our view, a more or less formal requirement that needs broad reading* – but whether it is consistent with the DSU rules and procedures (...). (Emphasis added)

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7 Exhibit EC – 5.
8 US Reply to Question 39, para. 5.
9 US’ Oral Statement, para. 42; US’ First Written Submission, para. 185; US’ Reply to Panel Question 41.
10 US’ Reply to Panel Question 41, para. 10.
12 Panel Report, *US – Section 301*, para. 7.50, footnote 657.
22. Thus, it is clear from this finding that even an implicit determination by the appropriate behaviour, such as the continuation of sanctions, would be covered by a “broad reading” of this requirement, in particular if the continuation occurs deliberately and is accompanied by respective statements.

23. Moreover, the interpretation of the word “determination” should be guided by the context of Article 23.2(a) of the DSU and the object and purpose of this provision. Contextually, Article 23.2(a) of the DSU has to be read together with Article 23.1 of the DSU, i.e. that a Member is “seeking the redress of a violation”: In such a situation, a Member shall not make a determination of violation except through recourse to the dispute settlement procedures. This provision as a whole, therefore, aims at preventing that a Member takes “the law in its hands” and seeks the redress of a violation on the basis of a unilateral determination. Finally, the importance of this general principle is confirmed by the title of this provision referring to the “strengthening of the multilateral system”. Thus, it is the WTO system as such which is at stake and one could, therefore, reasonably call the prohibition of unilateral action as a basic principle of the WTO.

24. The crucial importance of Article 23 has also been acknowledged by the Panel in US – Section 301:

   (...) the preservation of the specific guarantees provided for in Article 23 is of added importance given the spill-over effect they have on all material WTO rights and obligations.\(^\text{14}\)

25. In light of the overall context and the fundamental importance of Article 23 it is therefore justified to look at a Member’s behaviour as a whole when confronted with a respective situation.\(^\text{15}\) Thus, all relevant elements should be taken into account to assess whether a Member makes a unilateral determination of a violation when he seeks to redress a situation. This assessment must necessarily be comprehensive as not every policy statement may be equal to a “determination” of a violation or made with the purpose of “seeking a redress of a violation”. Conversely, if a WTO Member repeatedly and consistently states

\(^\text{14}\) Panel Report, US – Section 301, para. 7.94.
\(^\text{15}\) EC Oral Statement, para. 44.
that a violation by another Member exists and, in this context, this Member applies concrete measures against the other Member, it can be concluded that this Member is seeking a redress against a violation on the basis of a unilateral determination.

26. Applying these principles to the present case, there can be no doubt that the United States has made a unilateral “determination” of non-compliance of the EC measure. The United States has clearly stated that it does not consider the EC compliance measure to be sufficient. In addition to the 2005 Trade Policy Agenda quoted above, the United States stated, for instance, in the DSB meeting of December 2003 that

(... the United States failed to see how the revised EC' measure could be considered to implement the DSB recommendations and rulings.\(^\text{16}\))

27. If one takes a closer look at this statement it is evident that the United States expressed a definitive judgement about the EC measure and not a tentative opinion or some sort of “internal deliberation” or reflections. In other words, if a WTO Member submits that another WTO Member has not implemented the recommendations and rulings of the DSB does this WTO Member then mean that the other one is (not) in *compliance* with its WTO obligations? Or does this mean that this WTO Member is still *in the process* of internal deliberations? The answer is obvious: if a WTO Member denies that another Member has properly implemented, this WTO Member considers the other Member still being in violation.

28. If we look at the United States’ whole conduct there can equally be no doubt that the United States has made a “determination”. In addition to its recurrent statements that the EC compliance measure is WTO-inconsistent it deliberately *continues* to apply sanctions against the European Communities. Both, its public statements and its actions are fully coherent and they demonstrate that the United States has indeed made a “determination” of an alleged WTO violation by the EC compliance measure.

\(^{16}\) WT/DSB/M/159 of 15 January 2004.
29. The European Communities would not have been concerned about this US “determination” if had not occurred in the scope of Article 23 of the DSU. Thus, while it is of course true that WTO Members constantly make all kinds of notifications or statements\(^\text{17}\) and may also express themselves on what they consider not to be WTO-consistent, they do normally not make “determinations” while “seeking to redress a violation” by these day-to-day statements within the meaning of Article 23.1 DSU. Yet, as already demonstrated above, the United States is currently “seeking redress of a violation” by applying sanctions against the European Communities. This is what makes this case different from internal deliberations or other policy statements.

30. In this context, the European Communities would also reject the US assertion that it is “neither accurate nor appropriate to impute a “determination” from inaction”.\(^\text{18}\) Actually, this is a complete mischaracterization of the facts in this case. The United States is actively purporting that the EC compliance measure is WTO inconsistent. And, in addition, the United States is actively continuing to suspend concessions against the European Communities. Sanctions are being applied every day in the form of additional import duties – there is simply no way to consider this as “inaction”, just because stopping the sanctions would require some action. Thus, there is no basis whatsoever for the US assertion.

31. Furthermore, it is also important to recall that the European Communities adopted and notified its compliance measure over two years ago. To these two years one could add another three years since the European Communities notified its legislative proposal to the SPS Committee in November 2000. Still, the United States wants to make the Panel believe that it has not made any “determination” as to the WTO-consistency of the EC compliance measure. This begs the question, if the United States were correct, when would it make a “determination”? Probably the United States would never make any “determination” and, indeed, it would have not have any incentive to make such a “determination” as it would put at risk its convenient “lean-back-and-wait” attitude and continue to apply sanctions in the meantime.

\(^\text{17}\) US Reply to Panel Question 41, para. 8.
\(^\text{18}\) US Reply to Question 41, para. 8.
32. The European Communities also sees merits in China’s argument that the time-factor may be relevant for assessing when a “determination” actually has been made.\(^{19}\) The European Communities made a similar argument when pointing to the reasonable time frame in which an implementing Member can expect the other Party to bring an Article 21.5 proceeding.\(^{20}\) This argument does not ignore that this specific case raises complex scientific questions but up until now the United States had five years to consider these questions since the European Communities first notified its draft proposal to the SPS Committee.\(^{21}\) This is even more true if one compares these five years with the 90 days a compliance panel would have to decide whether a compliance measure is WTO-consistent under Article 21.5 of the DSU.

33. What we see, instead, is the attempt by the United States to declare its rights to apply sanctions sacrosanct and to refuse any responsibility for a prompt resolution (cf. Article 3.3 of the DSU!) of the dispute.

34. Finally, the European Communities would address the US assertion that accepting the EC position would be “ironic” as it would convert Article 23 from a “prohibition on making a determination into an obligation to make them”.\(^{22}\) There is nothing “ironic” in this. Article 23 in conjunction with Article 22.8 of the DSU does oblige a retaliatory Member to take note of a compliance measure and to decide if the continued application of sanctions is still justified. By virtue of these provisions the United States is under a special legal obligation. If the United States truly wanted to reflect further before making any “determination” or initiating a procedure under Article 21.5 of the DSU, it could have suspended the application of sanctions and taken all the time it wanted before coming up with any conclusion on the EC compliance measure. Furthermore, Article 23 of the DSU prohibits to make a unilateral determination of non-compliance. Conversely, nothing prevents the United States under Article 23 of the DSU to

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\(^{19}\) China Third Party Submission in WT/DS320 and WT/DS321, para. 42.; China Oral Statement, para. 11.

\(^{20}\) EC Oral Statement, paras. 77.

\(^{21}\) Just as a reminder, the European Communities was only granted a reasonable period of time 15 months to come up with a scientific evidence. Thus, a review that takes place over almost 60 months by now does not look quite as “reasonable”.

\(^{22}\) US Reply to Question 41, para. 10 (Emphasis in the original).
make a unilateral determination of compliance. Thus, unlike what the United States pretends Article 23 of the DSU does not prohibit any “determination”.

35. For all these reasons, the European Communities therefore considers that the United States has made a unilateral “determination” of an alleged violation with regard to the EC compliance measure within the meaning of Article 23.2(a) of the DSU.

2. **Article 21.5 of the DSU**

36. The European Communities argues that the United States was obliged if it disagrees with the EC compliance measure and in the circumstances of the present case, to launch a compliance proceeding against that measure on the basis of Article 23 read together with Article 21.5 of the DSU. Under Articles 23.1 and 23.2(a) a Member shall have recourse to dispute settlement in accordance with the DSU in case it seeks to redress a violation and it has made a determination that a violation has occurred. The special dispute settlement procedure under the DSU in a compliance situation is Article 21.5 of the DSU. By its lean-back-and-wait-attitude the United States failed to respect these procedures.

37. The United States argues that Article 21.5 of the DSU does not apply since there is no “disagreement” between the parties regarding the WTO consistency of the compliance measure in the absence of a US opinion on the EC measure. Moreover, an Article 21.5 proceeding does not contain any deadline. Finally, Article 21.5 of the DSU is not an exclusive proceeding but the WTO Agreement provides for several means on how to proceed.

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23 EC First Written Submission, paras. 50 et seq., 62 et seq.; EC Oral Statement, para. 46.
24 US First Written Submission, para. 194; US Oral Statement, para. 36; US Reply to Panel Question 48 para. 20
26 US First Written Submission, paras. 199 et seq.; US Oral Statement, paras. 34, 38.
38. The European Communities will address each of these arguments in turn. In addition, the European Communities will briefly comment on the US replies regarding the possibility of a self-initiated Article 21.5 proceeding.

\textit{i) The term “disagreement”}

39. The term “disagreement” is defined as “a refusal to accord or agree, difference of opinion, quarrel”.\textsuperscript{27} The United States’ attitude towards the EC compliance measure cannot escape this basic definition. Indeed, from the very beginning the United States “refused to agree” with the European Communities about the consistency of the EC compliance measure. This has not only been demonstrated by the various official statements made by the United States and, which as demonstrated above, lead to the conclusion that the United States made an unilateral “determination”. Moreover, the United States also expresses its disagreement by the continuation of the application of sanctions. Indeed, it is hardly conceivable that the United States had continued the application of sanctions had it agreed with the European Communities that the implementing measure was fully WTO consistent.

40. It goes without saying that the European Communities very much would have liked to see that the United States agreed with its compliance measure. However, this has not been the case. It is therefore somehow ironic that the United States even today submits that there is no “quarrel” between the United States and the European Communities about the EC compliance measure. If this were actually true one could reasonably ask why both parties find themselves in front of this Panel.

41. In this context it is also quite remarkable that during the first substantive meeting with the Panel neither Canada nor any of the third parties doubted that there was a “disagreement” between the European Communities and the United States regarding the WTO consistency of the EC measure. Indeed, Canada and the third parties were just stating the obvious which, however, in view of the US statement should be re-emphasized in this context.
42. The European Communities does not agree with the United States’ assertion that the EC assumption of a “disagreement” conflicts with its interpretation of the term “determination” under Article 23.\textsuperscript{28} The United States essentially argues that if a “determination” under Article 23 could be inferred from a “disagreement” the suspending Member would be in an impossible situation as “it must breach Article 23 either through not invoking Article 21.5 or through invoking Article 21.5”.\textsuperscript{29}

43. This is a false conclusion. First, Article 23 of the DSU does not apply to any sort of “disagreement” but only in case of a “determination” of a violation which a Member is “seeking to redress”. This is exactly what the United States is currently doing by continuing to suspend concessions against the European Communities. Conversely, had the United States suspended the application of sanctions it would arguably not have been within the scope of Article 23 of the DSU because it would, arguably, not have sought to redress an (alleged) violation. Second, in any event the United States fails to recognize that Article 23 contains an explicit reference to dispute settlement proceedings, which includes Article 21.5 of the DSU. Thus, Article 23.2(a) of the DSU prohibits unilateral determinations of a violation “except through recourse to dispute settlement in accordance with the rules and procedures of this Understanding”. Thus, had the United States invoked a procedure under Article 21.5 of the DSU it would have fully satisfied Article 23.2(a) of the DSU.

44. To conclude on this point: the United States submits that “if there is no “disagreement” between the parties, there is certainly no “determination” as to the WTO-consistency of a measure.”\textsuperscript{30} However, the correct reading in this case would be that since there is a “determination” as to the WTO-consistency of a measure there is also a “disagreement” between the parties.

\textit{ii) The issue of “deadline” under Article 21.5 of the DSU}

\textsuperscript{28} US Reply to Question 57, paras. 41 \textit{et seq}.
\textsuperscript{29} \textit{Ibid.}, para. 41.
\textsuperscript{30} \textit{Ibid.}, para. 42.
45. By its second objection the United States alleges that the European Communities’ interpretation of Article 21.5 would impose a “deadline” for the suspending Member. As the European Communities has made clear in its Oral Statement, the merits of such an objection could probably be discussed if the EC compliance measure had been recent. However, this is not the case: the European Communities notified the first draft of the measure as long as five years ago. The Council Directive 2003/74/EC was subsequently adopted two years ago. And during all this time the United States apparently leaned back and did nothing. In these circumstances it is certainly not asking too much that a WTO Member which contests the compliance measure of another Member and applies at the same time sanctions against that Member, makes an effort and launches a compliance proceeding. This, at least, would have given the possibility to the European Communities to know specifically the reasons why the United States objects to the EC implementing measure.

46. Conceptually, it is also misplaced to interpret “as a deadline” the argument whereby a Member should in case of a disagreement within a reasonable timeframe initiate a compliance procedure. Of course, the DSU does not contain such a deadline for an Article 21.5 proceeding even though the DSU is guided by the principle that disputes should be settled “promptly”, Article 3.3 of the DSU. For instance, in a compliance procedure, Article 21.5 of the DSU provides that a Panel should determine the consistency or inconsistency of an implementing measure within 90 days. The 90 days could therefore be considered as a reasonable period also for a retaliating Member to decide on the WTO consistency of a compliance measure. Moreover, every treaty must be performed in good faith, Article 26 of the Vienna Convention. Thus, depending on the circumstances of a case, a WTO Member contesting the WTO-consistency of a measure can be expected within a reasonable timeframe to submit the dispute to the competent bodies, i.e. the original Panel under Article 21.5. If a Panel can be asked to decide whether there is compliance in 90 days, it seems hardly acceptable that a retaliating Member sits back for eight times as long (i.e. two

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31 EC Oral Statement, paras. 47 et seq.
32 This is of course not a matter of “a day or a week” as the United States suggests, cf. US Reply to Question 40, para. 7.
years) and still argues that it cannot make up his mind as to the consistency of the measure. Thus, in the circumstances of the very long time-period that has elapsed in the present case, the question of when exactly too much time has elapsed does not pose itself.

47. This is even more relevant in a case like this one which involves the application of sanctions. In such a scenario it is difficult to accept that a WTO Member continues endlessly to apply sanctions against another Member on the basis of a unilateral determination of non-compliance and, at the same time, rejects any responsibility to find a prompt solution to a dispute in accordance with the relevant DSU rules. This, again, is certainly a convenient policy attitude but it is also in plain contradiction to the text and the spirit of the DSU.

iii) Article 21.5 and alternative means

48. The European Communities has some conceptual difficulties in understanding the US argument on why Article 21.5 is not the exclusive procedure under the DSU to resolve a disagreement as to the WTO consistency of the measure: On the one hand, the United States seems to argue that Article 21.5 of the DSU does not apply at all since there may be other alternative means available. On the other hand, the United States points to the text of Article 21.5 of the DSU which refers to “these dispute settlement procedures” thus indicating that Article 21.5 applies in any event but is not limited to a panel compliance proceeding.

49. In the view of the European Communities, Article 21.5 of the DSU provides for a specific panel proceeding in case there is a disagreement about the WTO consistency of a compliance measure. The wording of Article 21.5 of the DSU is unequivocal to this effect: such disagreement “shall be decided through recourse to these dispute settlement procedures (…)”. Thus, Article 21.5 of the DSU imposes a positive obligation to resolve dispute on a compliance measure by having recourse to the respective dispute settlement proceedings.

33 Actually, this proceeding demonstrates well enough that the United States is perfectly capable to argue why it considers the EC measure as WTO inconsistent.
34 US Reply to Question 56, para. 39.
50. This interpretation is contextually confirmed by Article 3.3 of the DSU whereby disputes should be settled “promptly”. In the specific compliance situation, the drafters of the DSU had provided an accelerated procedure under Article 21.5 of the DSU in order to resolve quickly a protracted dispute. As it is considered in the complaining party’s interest to have a quick solution to a dispute the complaining party shall initiate a fast-track procedure if it disagrees with a compliance measure.

51. Against this background, it appears somewhat disingenuous for the United States to consider a proceeding under Article 21.5 of the DSU solely as a matter of political opportunity in particular if at the same time it assumes the right to continue to sanction the implementing WTO Member. This is not only contrary to the wording of Article 21.5 of the DSU but also against the object and purpose of this provision.

52. Let us consider, for instance, the US example whereby a complaining Member would prefer to initiate a totally new Panel proceeding against a compliance measure combined with a non-compliance measure instead of a proper Article 21.5 proceeding.\(^{35}\) What the United States is essentially arguing is that a WTO Member which applies sanctions may take all the time in the world to choose the procedure and the timing which is “most suited to the particular situation”.\(^{36}\) According to the United States, a retaliating Member could thus wait for years to initiate a dispute against a complying Member just when it best suits the retaliating Member. Needless to say, the United States would in the meantime continue to apply sanctions as if nothing had happened.

53. This is quite an extraordinary denial of any responsibility for the well-functioning of the dispute settlement system and the prompt settlement of disputes.

54. It goes without saying that in such a situation there is only one single “procedure most suited to the particular situation”, which is the compliance proceeding under Article 21.5 of the DSU. This is even more true in case of the application

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\(^{35}\) US Oral Statement, para. 38.

\(^{36}\) Ibid.
of sanctions. Conversely, it runs diametrically against the object and purpose of the dispute settlement system that a WTO Member continues to apply sanctions against another WTO Member solely on the basis of a unilateral determination of non-compliance. As we have said many times before, the US position is guided by the simple mantra to declare its rights sacrosanct and not to accept any legal obligations which would contradict its convenient lean-back-and-wait position.

55. In this context, the European Communities would also refer to the very revealing US reply to Questions 46 and 42 of the Panel. The Panel asked why the United States did not initiate an Article 21.5 proceeding if it had been interested in a prompt resolution of the dispute. The United States answered that it would have liked a prompt resolution of the issue, i.e. “to have the import ban on its products lifted”.\(^{37}\) In addition, the United States submits once again that it was under “no obligation” to initiate an Article 21.5 proceeding.\(^{38}\) Furthermore, the United States submitted that “it would seem odd to read the DSU as saying that a Member that has already been found to be in breach of a covered agreement and that has maintained that breach past the end of the reasonable period of time should have a right to proceedings that are more expedited than the member who has been suffering nullification and impairment during that entire time period”.\(^{39}\)

56. Three comments apply in this respect:

57. First, it is important to underline the open admission by the United States that it considers that the only solution to this dispute would be the lifting of the import ban. Yet, as the European Communities has recurrently reiterated, this is not what the SPS Agreement requires nor what the Appellate Body found. The European Communities has fully complied with its obligations once it is demonstrated that the SPS measure is definitively or provisionally justified. This is exactly what the European Communities has done by its Directive 2003/74/EC. Instead, the United States is obviously seeking to use its retaliatory rights to leverage a solution to which it is not entitled.

\(^{37}\) US reply to Question 46, para. 16.
\(^{38}\) \textit{Ibid}, para. 17. US Reply to Question 42, para. 11.
\(^{39}\) US Reply to Question 42, para. 11.
58. Second, if it were true that the United States were interested in a quick resolution of a matter, it would have been logical to initiate an Article 21.5 proceeding independently of whether or not the United States would see a “legal obligation” to do so. In other words, the alleged absence of a legal obligation does not explain why the United States did not act despite the undisputed possibility to do so. The evasive US answer, therefore, does not give a proper response to the Panel’s question.

59. Third, probably, the true motivation to the US attitude may be found in the last sentence of its reply to Question 42 which seems based on an “eye for an eye, tooth for a tooth” mentality: Since the import ban has been damaging the United States for so long, the United States is now paying back in kind by protracting its sanctions against the European Communities. The European Communities has serious doubts that this is in the spirit of the DSU and the WTO Agreement as a whole. And it is, in any event, not a relevant legal argument.

60. Finally, the special procedure under Article 21.5 is also not overridden by any alternative means such as good offices, conciliation, mediation or arbitration under Articles 5 and 25. The procedures under Article 5 are “undertaken voluntarily if the parties to the dispute so agree” and they do not result in a binding outcome. Thus, if the implementing Member refuses to engage in these procedures there is nothing a complaining Member could do. The same is true for the arbitration under Article 25 which requires a “mutual agreement of the parties”. Consequently, nothing in these procedures indicates that the special compliance procedure under Article 21.5 is in any way overridden.

iv) The self-initiation of an Article 21.5 proceeding by the implementing Member.

61. The European Communities has repeatedly argued that it is not possible or meaningful to initiate a compliance review against its own implementing measure. One of the central arguments in this respect has been that the DSU is based on a contradictory proceeding whereby a complaining party alleges a WTO-violation against another party. Conversely, the DSU does not provide for
a situation where a “complaining party” alleges the WTO-consistency of its own measure.  

62. Against this background, the European Communities appreciates that the United States acknowledges these basic difficulties as set out by the European Communities by stating that “it is difficult for a Member to have to demonstrate the negative – that there is no inconsistency”. 

63. On the other hand, the European Communities disagrees with the US Reply to Question 45 concerning the mechanism of a self-initiated Article 21.5 proceeding. In this context, the European Communities would draw the Panel’s attention to the lack of substance of the US replies to EC Questions 2 to 6. It may appear somewhat ironic that the United States and the European Communities seem to have reversed the roles since the first and only self-initiated Article 21.5 proceeding in the Bananas-case. At the time, the United States vigorously opposed the establishment of the compliance Panel as requested by the European Communities. In this respect, the US representative in the DSB stated that “it was not clear what the EC was requesting as it could not request a panel to rule against its own measures”. 

64. The European Communities would agree with this last US statement and given the experience of the Bananas-case, which clearly showed that the whole approach does not work, the European Communities – as well as other WTO Members - never proposed the adoption of the report by the DSB. Conversely, it is rather surprising to read in the US reply to the Panel Question that the European Communities as initiating the proceeding would be the “complaining party” within the meaning of Article 6 of the DSU. But, to paraphrase the US statement in the DSB meeting of 1999, against what would the European Communities complain? And against what should the Panel rule in the absence of a complaint? In case of a self-initiated proceeding there are no good answers to these questions. Furthermore, the European Communities would recall that

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40 EC Reply to Question 1, paras. 1 et seq.
41 US Reply to Question 62, para. 56.
42 WT/DSB/M/53.
there are strong doubts regarding whether, under Article 1.1 of the DSU, the DSU would at all apply to such a self-initiated procedure.43

II. THE UNITED STATES’ CONTINUED SUSPENSION OF CONCESSIONS AND RELATED OBLIGATIONS IS IN VIOLATION OF ARTICLE 23.1, READ TOGETHER WITH ARTICLES 22.8, 3.7 OF THE DSU

65. The European Communities has already explained why by the US continued application of sanctions against the EC compliance measure falls within the scope Article 23.1.44 This provision requires to follow the rules and procedures of the DSU including Article 22.8. Article 22.8 in turn obliges the United States to cease the application of the sanctions as the original violating measure had been withdrawn and the compliance measure has not been found to be WTO-inconsistent. In the absence of a measure which has never been multilaterally found WTO-inconsistent there exists no basis for the continued suspension of concessions and related obligations.

66. The core of the US defence is that it may continue to apply sanctions until the DSB authorization has been formally terminated.45 In this context, the United States also denies that the principle of good faith applies at all to dispute settlement proceedings.46

67. The European Communities will address both of these issues in turn.

1. The scope of the DSB authorization

68. The European Communities is still puzzled by the US assertion that the continued application of sanctions against the EC compliance measure is justified on the basis of a DSB authorization granted in respect of the original EC measure.

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43 EC Reply to Question 1, para. 5 et seq.
44 EC First Written Submission, paras. 28 et seq., 73; EC Oral Statement, paras. 27 et seq., see above paras. 6 et seq.
45 US Reply to Question 39, para. 5, US Reply to Question 51, para. 31; US Reply to EC Question 13, para. 9; US First Written Submission, para. 204.
46 US Reply to Question 61, para. 48.
69. The European Communities, of course, understands that the United States disagrees that the continued application of the sanctions is related to the EC compliance measure. However, given the undisputable fact that the original EC measure has been removed\(^{47}\) this would leave as the only logical conclusion that the United States is currently applying sanctions against a non-existent measure. Or, in other words, the United States is applying sanctions for the beauty of a DSB authorization irrespective of whether or not the original EC inconsistent measure still exists or has been removed by a compliance act. The European Communities very much doubts that such an absurd conclusion really advances the US defence in this case. In fact, this conclusion would be in plain contradiction with the very purpose of sanctions, namely to rebalance rights and obligations and to induce compliance in the light of a current WTO violation.\(^{48}\)

70. This brings us back to the more reasonable assumption that the United States currently continues to apply sanctions because it considers the EC compliance measure as insufficient.\(^{49}\) It suffices to recall the United States in its 2005 Trade Policy Agenda:

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\text{The United States maintains its WTO-authorized sanctions on EU products because the United States fails to see how the revised EC measure could be considered to implement the recommendations and ruling of the DSB in this matter.}\(^{50}\)
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71. This statement does not leave any doubts about the true motives of the US continued application of the sanctions irrespective of the US attempts to re-qualify its sanctions for the purpose of this proceeding.

72. This raises, however, the question how the continued application of an “old” DSB authorization can be justified against a “new” measure on which the DSB authorization is not based. At least in this case where the new measure has never properly been found to be WTO-inconsistent the answer to this question is that it cannot be justified.

\(^{47}\) Even the United States concedes that a ban would be a “different measure” depending on the underlying risk assessment, US Reply to Question 54, para. 36.

\(^{48}\) Quite remarkably, the United States could not provide any good answer to this conclusion in its Reply to the EC Question 13, para. 9.

\(^{49}\) See also paras. 8 \textit{et seq.} above.
73. The European Communities does, of course, not deny that the DSB authorization has not formally been removed. However, under Article 22.8 of the DSU it does not matter whether the DSB authorization has formally been removed or not, a procedural step which the DSU does not even foresee. Rather, under Article 22.8 of the DSU it matters whether the suspension of concessions and related obligations may still be “applied” (pursuant to a DSB authorization). Article 22.8 of the DSU is unequivocal in this respect: the suspension of concessions and related obligations may only be “applied” until the inconsistency of the measure has been removed.

74. This is confirmed by the wording in Article 22.8 of the DSU which refers to a “measure found to be inconsistent with a covered agreement”. Even though it is formulated in the passive the only way to “find” a measure to be WTO-inconsistent under the DSU is through the multilateral procedure. Thus, it is not possible to apply sanctions under Article 22.8 of the DSU and the other relevant provisions under the DSU (Article 23 of the DSU!) solely on the basis of a “unilateral finding” of inconsistency. In the same vein, the continuation of sanctions cannot be based on a unilateral finding of inconsistency of the compliance measure.

75. Furthermore, the European Communities would re-emphasize the self-executing nature of Article 22.8 of the DSU. Thus, the termination of the application of sanctions under this provision does not depend on a specific finding of the DSB or a withdrawal of the DSB authorization. Rather, once the conditions under Article 22.8 of the DSU are met – including in the presence of an unchallenged compliance measure – the application of suspension “shall” automatically stop. As the European Communities has already explained in its First Written Submission51 the mandatory and non-discretionary language of Article 22.8 of the DSU does not provide a retaliating Member with a possibility to continue the application of sanctions. This logic is confirmed by the temporary nature of the suspension of concessions or obligations.

51  EC First Written Submission (US), para. 95.
2. The principle of good faith

76. The United States has argued that “there is no presumption of compliance or good faith in WTO dispute settlement that attaches to measures taken by WTO Members”\(^{52}\).

77. In its Reply to Question 61 the European Communities has set out clearly how the principle of good faith and the presumption of compliance are interrelated\(^{53}\). In addition, in its reply to Question 4, the European Communities has explained in detail that the scope of the principle of good faith cannot be reduced to the mere issue of burden of proof as the United States asserts\(^{54}\).

78. That said, it is quite remarkable that the United States in stark contrast to Canada and third parties in this proceeding denies that the principle of good faith applies generally in WTO dispute settlement proceeding. The European Communities considers that such a radical position is not supported by the general public international law, which also applies to the WTO, as for instance expressed in Article 26 of the Vienna Convention of the Law of the Treaties.

79. In this context, the European Communities would also recall the specific circumstances in which the compliance measure had been adopted. These circumstances clearly demonstrate that the invocation of the principle of good faith and the presumption of compliance by the European Communities is not only an abstract idea but it is corroborated by the concrete facts. First, the European Communities would refer to the intensive procedural steps it undertook to analyze the risks of hormones used for growth promotion purposes in meat. These steps have been set out in its Oral Statement\(^{55}\) and we will refer to them in a more comprehensive form in the second Part of this submission. Secondly, the European Communities made every effort to discuss with the United States the background of the new compliance measure. In this respect, the European Communities regrets very much the dismissive attitude the United States adopted.

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\(^{52}\) US Reply to Question 61, paras. 48 et seq.
\(^{53}\) EC Reply to Question 61, paras. 212 et seq.
\(^{54}\) EC Reply to Question 4, paras. 26 et seq
\(^{55}\) EC Oral Statement, paras. 91 et seq.
in this proceeding\textsuperscript{56} regarding this cooperation between the European Communities and the United States. However, it remains a fact that the European Communities tried to work closely with the United States throughout the implementing phase.

80. Thirdly, the European Communities would recall the US attitude after the European Communities adopted and notified to the DSB its compliance measure. In essence, the United States stated several times in a relatively blunt manner that this measure was not good enough and then, most importantly, continued to apply sanctions. And this situation still continues today. However, in the absence of a concrete challenge by the United States against the EC compliance measure and in the light of the months and years that have passed since the measure was prepared, discussed and adopted, the European Communities believes that it has every good reason to invoke the principle of good faith and the presumption of compliance for its implementing measure.

\textit{PART 2: The WTO-consistency of the EC compliance measure}

I. \textsc{Introduction}

81. The European Communities has made a direct claim under Article 22.8 on the condition that the Panel would not find on a violation of Article 23 of the DSU in conjunction with Article 22.8.

82. In its First Written Submission the United States puts forward a number of arguments against this claim. Essentially, these arguments all turn on the question of whether or not the European Communities has set out a \textit{prima facie} case that the measure which has been the object of the \textit{Hormones} ruling has actually been

\textsuperscript{56} US Reply to Question 38, para. 2, US Reply to Question 53, para. 34.
removed. The United States submitted, with its written and oral submissions as well as with its replies to the Panel’s questions, scientific arguments as to why, in its view, the European Communities’ compliance measure is not consistent with the DSB recommendation. The United States has also provided a long list of exhibits containing several papers and documents which it claims are relevant to its arguments and necessary to resolve the claim made in the alternative by the European Communities in this dispute.

83. This second written submission is, therefore, the first opportunity for the European Communities to reply to the arguments in detail and to exercise its rights of defence as regards these claims, in particular by providing in turn the necessary evidence in response to those advanced by the United States.57

84. The presentation of facts and discussion of legal arguments in the following sections will therefore concentrate on rebutting these arguments and in responding to the evidence they have appended to their written and oral submissions. It is given in order to allow the Panel to explore all the issues raised in these proceedings but is without prejudice to the European Communities’ position on the Panel’s terms of reference.58

II. FACTS

85. The European Communities, in its Oral Statement at the first substantive hearing as well as in a number of replies to the Panel’s questions, has described and explained the various steps undertaken to carry out the comprehensive risk assessment which led to the adoption of its implementation measure, i.e. the revised Hormones Directive 2003/74/EC.59 It seems useful at this stage, however, to briefly summarize them once again putting them in the broader context of the scientific developments on the pertinent issues during the relevant time period.

57 The argument made by the United States in its replies to Panel Question 64, paragraph 63 is without merit, because the Panel’s Working Procedures do allow the European Communities to submit evidence for purposes of rebuttals and in reply to questions and comments to questions by the Panel and the parties.

58 See EC Replies to Questions, paras. 239 and 242 (footnote 76).

59 See EC Oral Statement, at paras. 91 et seq.; also EC Replies to Question 16 paras. 76 et seq.; Question 17, in particular at paras. 85 et seq., Question 19, paras. 103; Question 22, paras. 124 et seq.
While it is important to link these developments back to the developments leading up to and including the Appellate Body decision in the *Hormones* case, the European Communities, contrary to the United States, does not consider it necessary to describe the latter once again in great detail as they have been sufficiently described in the *Hormones* decision.

A. Overview of Developments since the DSB recommendation on Hormones

86. To comply with the February 1998 DSB recommendation in the *Hormones* case, the European Communities launched immediately thereafter a process of carrying out a risk assessment in light of the very important clarifications provided by the Appellate Body. It is recalled that the *Hormones* case was the first to interpret the provisions of the *SPS Agreement*, in particular the provisions of Articles 3 and 5 thereof. It was the Appellate Body’s report in the *Hormones* case that for the first time shed light on what is and how to conduct a risk assessment for the purposes of the *SPS Agreement*.

87. As the Appellate Body found that the studies and other evidence presented by the European Communities was relevant but not sufficiently specific\(^{60}\), the objective of the compliance effort undertaken was not only to re-assess all existing and most recent data from any relevant source for the six hormones, but also to complement these data in particular in three respects, namely: a) on certain issues regarding specific health risks from residues in meat treated with hormones from growth promotion purposes, b) on risks arising from possible abusive use and difficulties of control, and c) on an appropriate risk assessment for melegenstrol acetate (MGA), which had not been carried out so far.

1. Gathering of complementary data

88. The European Communities took two main initiatives to gather the required complementary information: (1) it launched 17 specific studies, (2) it tried to collect information from all relevant sources, including from third countries,

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international scientific bodies and industry. All these steps were undertaken in full transparency and after consulting the relevant scientific committees and bodies that are responsible under Community law to conduct this kind of assessment.

(a) The 17 studies

89. To respond to the criticism of the Appellate Body on the scientific basis of the EC hormone ban, the European Communities launched, soon after February 1998, 17 scientific studies which were designed to improve and complement the current scientific knowledge about these hormones. These studies involved several well known scientists and research institutions from Europe and the Untied States and required spending a very substantial amount of money for their completion by the European Community. The results of practically all of the studies were presented in international scientific conferences and have been published in leading peer-reviewed scientific journals.61

90. It is important to understand, however, that although the studies were intended to provide as complete a new data base for the complementary risk assessment as possible, the breadth and complexity of the scientific issues at stake meant that, as it will be explained below, the studies could finally not address all the gaps in our scientific knowledge.

91. As is clear from Exhibit EC – 6 the studies focussed on a number of issues, but in particular on toxicological and other adverse effects from residues in meat treated with hormones for growth promotion, on residue analysis, residue characterisation, and possibilities of abuse and lack of control aspects that may have adverse effects on humans, animals and the environment.

92. The studies were finalised over the course of 2001. The studies and/or the peer reviewed publications have been submitted to the Panel in reply to Panel Question 16.62

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61 See Exhibit EC – 10. Reference to the proceedings of this conference has already been made in the EC Reply to Panel Question 16, paragraph 79, footnote 25.

62 Exhibit EC – 6.
(a) Information from third countries, international scientific bodies and industry

93. In order to have available complete, pertinent and up to date information for the new risk assessment and to allow a peer review of past risk assessments, the European Communities sought to obtain all relevant information and assessments from several pertinent sources.

94. In April 1998, it contacted the regulatory authorities of third countries in which the use for growth promotion purposes of the six substances in question has been authorised, namely the United States, Canada, Australia and New Zealand. The letters that were sent and the replies received have been submitted to the Panel in reply to Panel Question 32.63

95. The European Communities did not receive the requested information from these countries. It is particularly important to underline the attitude of the United States and Canada. It is clear from these letters that the United States initially refused to provide the information and data saying essentially that they are business confidential information, then, on second thoughts, appeared to show some openness to provide some of the data under certain conditions, and finally never supplied what it promised to do. The same applies to Canada which replied by saying that the information was confidential and, therefore, could not be released under domestic law. Australia replied along the same lines, whilst New Zealand did not reply at all, but seems to have had the same concerns.64 It is important to note that the raw data on residues for all these hormones which are held by the United States authorities are those that served also as a basis for the Codex/JECFA’s evaluation of these hormones in 1988 and 1999.65

96. In May 1998, the European Communities contacted the FAO/WHO Secretariat of the Joint Expert Committee on Food Additives (JECFA) to request the data on the basis of which JECFA had carried out its 1988 risk assessment. The FAO/WHO

63 Exhibit EC – 9.
64 See New Zealand Replies to EC Question 15.
65 As the EC explained with its letter of 11 November to the Panel, these data are at the basis of JECFA’s evaluations and most, if not all, of them are not published. So they can be retrieved only from the US authorities or the industry. But the EC has no means to compel the industry, especially when it is located abroad, to provide these data.
Secretariat advised that the raw data and other relevant documentation were no longer available as they were “either returned to the submitter or destroyed after the evaluations were completed.” In a later letter it pointed out that most of the information that was evaluated on these substances in 1987 was in the form of published papers and referred to the fact that “many scientific advances had been made since 1987.” However, as it is explained in the letter of the European Communities to the Panel of 11 November 2005, it appears that at least the residues data for the three natural hormones used in the 1999 opinion of JECFA are the same as those used in 1988.

The European Communities also inquired about JECFA’s reasons for deciding to re-assess the three natural hormones and for not (re-)assessing the three synthetic hormones. Most importantly, however, the European Community invited JECFA to await the results of the 17 studies which it had already launched before proceeding with the re-assessment of the three natural hormones. However, the FAO/WHO declined the invitation by the European Communities to await the results of the 17 studies before carrying out a new risk assessment on the three natural hormones without any valid justification.66 The letters that were sent and the replies received have been submitted to the Panel in reply to Panel Question 32.67

Finally, in February 1999, the European Communities published in its Official Journal an open call to all companies and interested parties, inside and outside the European Union, requesting scientific documentation on the six hormonal substances that is available to the companies selling and distributing the

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66 Thus, in the report of the 11th session of the Codex Committee on residues, held in Washington D.C., on 15 – 18 September 1998, ALINORM 99/31, it is stated the following: “The question was raised as to why the natural hormones (estradiol-17β, progesterone, and testosterone) had been placed on the agenda of the JECFA for re-evaluation. It was pointed out that they were placed on the agenda at the initiative of the JECFA Secretariat to ensure that all the latest information had been evaluated. On the evaluation of natural hormones, the European Commission pointed out that it had written to the JECFA Secretariat in order to make JECFA aware that a number of substantial studies were currently being prepared by the EU and had requested that the JECFA evaluation be deferred to a later JECFA meeting. The European Community, therefore, reiterated the request to defer the JECFA consideration.” (at para.125).

67 Exhibit EC – 9.
substances, but is not in the open literature. The European Communities received no reply to that call for submission of data.

99. The European Communities considers, therefore, that in the circumstances of this case it had done all it could to obtain any relevant information from all pertinent sources in time for the purposes of its risk assessment.

3. Scientific Assessment by the SCVPH

100. In November 1998, the European Communities mandated its Scientific Committee on Veterinary measures relating to Public Health (SCVPH), which was the scientific committee responsible on these issues under Community law applicable at the time, to address the potential risks to human health from hormone residues in bovine meat and meat products treated with the six hormones for growth promotion.

101. The SCVPH was part of a group of altogether 9 scientific committees which were set up under EC legislation to provide expert advice on scientific issues to the European Communities. The SCVPH was competent for scientific and technical

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69 The competences of the SCVPH have since 2003 been absorbed by the European Food Safety Authority (EFSA). The EFSA was established by Regulation (EC) No 178/2002 laying down the general principles and requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety O.J. L 031, 1.02.2002 p.1. EFSA came into full operation in July 2003.
70 The Committees comprised a Scientific Steering Committee which was responsible for overall scientific co-ordination and for multi-disciplinary scientific questions and 8 Scientific Committees which were independently responsible for giving advice in their particular field of competence. Together, the 9 Scientific Committees covered all areas of food safety, including primary products of animal and plant origin, animal health and welfare, cosmetics and non-food consumer products, medicinal products and medicinal devices, as well as all issues concerning toxicity, ecotoxicity and the environment. Members of the Committees were appointed in their individual capacity (ad personam) and were not paid for their work. Only their travel and subsistence expenses were reimbursed and they received an indemnity to cover small costs associated with their preparatory work. The Committees were established by Commission Decision (97/579/EC of 23 July 1997) which set out the essential principles which guide the work of the Committees: excellence, independence and transparency.

Excellence: The call for expression of interests, open to scientists from throughout the world, resulted in over 1000 responses. Selection Committees under the chairmanship of internationally respected scientists established a list of the most competent scientists from which the Commission nominated the members of the Scientific Committees on the basis of their individual field of competence and of the scientific expertise required for each Committee. The procedure was designed to ensure that
questions concerning consumer health and food safety related to the production processing, and supply of food of animal origin. It comprised 15 members with particular expertise in veterinary and human medicine, public health, microbiology, virology, epidemiology, immunology and toxicology.71

102. The timing of the mandate is explained through the time constraints imposed by the WTO ruling. The European Communities had been accorded a reasonable period of time for implementation of 15 months, ending on 13 May 1999. Thus, even in the absence of certain information that was still to come in, namely the results of the 17 studies which had different starting and completion time-frames in view of the specificities of each study, the European Communities requested the SCVPH to carry out a risk assessment on the basis of all currently available scientific evidence. The mandate contained specific questions, which the SCVPH was requested to reply to, and which in part addressed specific points that had been raised by the WTO dispute settlement bodies in the Hormones decision. In particular, the SCVPH was asked to comment on the issue of residue specificity, dose-response assessment, and of sufficiency of evidence (for further discussion see below).

members of the Scientific Committees would have a high level of experience in a relevant professional and international context and appropriate experience in risk assessment.

Independence: Members were required to declare any potential conflicts on interest to the Commission on an annual basis. Such declarations were made public at the discretion of the Members. Furthermore, members of scientific Committees and their working groups were required to declare at the beginning of each meeting any potential conflict of interests which could be regarded as prejudicial to their independence as concerns the topics on the agenda of that meeting. The Committee decided on a case by case basis on the extent of the member's participation in the work. A member who was not able to act independently was not invited to be rapporteur or chairperson and may not seek to influence the conclusions. Declarations of interests were recorded.

Transparency: In addition to an open procedure for the identification and selection of members, extensive use was made of the Internet to provide rapid and direct access to information on the Committees. This included the draft agendas in advance to plenary sessions, minutes and opinions as soon as they were adopted. Published opinions included a full scientific reasoning as well as the literature references upon which they were based. This procedure allowed all interested persons to follow the activities of the Scientific Committees closely and renders scientific advice transparent.

71 The names of the members, the agendas and the opinions of the committee are publicly available under http://europa.eu.int/comm/dg24/health/sc/index_en.html
103. In accordance with its rules of procedure, the Committee established a Working Group under the chairmanship of one of its Members. The Committee identified the fields of expertise it considered necessary to respond to the mandate and decided on the composition of the Working Group consisting of specialists selected on the basis of their scientific expertise in the different scientific areas concerned. The Working Group met several times and prepared a draft report which was subsequently presented by the rapporteur to the SCVPH. The SCVPH discussed the issue in detail at its Plenary session on 29-30 April 1999 and adopted its opinion unanimously (hereinafter “1999 Opinion”). The 1999 Opinion took account of all pertinent scientific information available at the time, including JECFA’s revised assessment of the three natural hormones oestradiol 17β, testosterone and progesterone that had been issued in February 1999.

104. As already explained (and will be further developed below) the 1999 Opinion concluded that a risk to the consumer had been identified with different levels of conclusive evidence for the six hormones evaluated. In particular, the SCVPH identified oestradiol 17β to be a complete carcinogen. As for the other five substances, the SCVPH on the basis of the available toxicological and epidemiological data concluded that the current state of knowledge did not make it possible to give a quantitative estimate of the risk to consumer. The 1999 Opinion also pointed to the specific risks arising of an abusive use of the hormonal substances in question.

105. Subsequently, the SCVPH was twice requested to review its opinion in light of new assessments carried out by other bodies or institutions and new evidence.

106. Thus, the Committee was asked in 2000 to advise whether any recent scientific information provide any new information or interpretations which would lead the SCVPH to revise its 1999 Opinion. The request was specifically intended to review two reports that had come out in the meantime, namely the December 1999 report of the Committee on Veterinary Medicinal Products (CVMP) on 17β-

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72 The Working Group established to assist the SCVPH was composed of 9 independent specialists, 4 of which are well known scientists from the USA.

oestradiol and progesterone for zootechnical and therapeutic purposes,\textsuperscript{74} and the October 1999 report of the UK Veterinary Products Committee sub-group.\textsuperscript{75} As regards the former, it should be noted that the nature of the assessment carried out by the CVMP is different in that it exclusively focuses on potential adverse effects of oestradiol and progesterone when used for zootechnical and therapeutic purposes, not for possible adverse effects on humans from exposure to hormone treated meat. As the Appellate Body correctly found in the \textit{Hormones} case, when used for the therapeutic or zootechnical purposes, the said hormonal substances are actually applied in completely different ways and doses, thus altering any assessment of potential adverse effects. Moreover, the opinion of the CVMP did not examine all the six hormones but only oestradiol and progesterone, nor did it examine the potential for misuse or abuse for these two hormones. This said, the SCVPH examined in its 1999 Opinion the report issued by the CVMP and came to the conclusion that it could not share its findings to the extent they were relevant for the purposes of its risk assessment.

107. As regards the October 1999 report of the UK Veterinary Products Committee sub-group, it should be noted that this is in the nature of a review or second opinion report (thus not based on new scientific evidence), directly reacting to the 1999 Opinion of the SCVPH.\textsuperscript{76} It should also be explained that under the applicable Community rules any Member State is entitled to carry out its own assessment or review of chemical or veterinary substances, even if they are subject to review at the same time at Community level. In the present case, only the UK authorities decided to carry out this review once in 1999 and again in 2005, but none of the other Member States have done so. It should also be noted that the UK authorities have always shown a continued interest on these substances since a long time ago (see, e.g., the Lamming reports). What is also more important to note is that the UK Government did not vote against the adoption of the new Directive 2003/74/EC when it was presented as a draft in the European Council, despite the fact that it had at that time received the 1999 report from its Veterinary...
Products Committee. This means that the responsible UK Government drew the appropriate risk management conclusions on the basis of all available opinions and reports and not only on that of its 1999 Veterinary Products Committee.

108. The SCVPH reviewed and discussed the 1999 UK report, the 1999 JECFA report, as well as other available evidence from new scientific publications and concluded that they did not provide convincing data and arguments demanding revision of its conclusions drawn in the 1999 Opinion. The SCVPH report to this effect was adopted at the SCVPH’s plenary session of 3 May 2000 (hereinafter “the 2000 Opinion”).

109. In 2002, the SCVPH was again asked to review recent scientific information and evidence, as the adoption of Directive 2003/74/EC was coming closer. Obviously, the responsible risk management authorities of the European Communities wished to be updated and reassured that there was a clear rational relationship between the measure about to be adopted and the risk assessment of these six hormones when used for animal growth promotion. The new risk assessment request was specifically aimed at the results of the 17 studies that had come out in the meantime, but invited the SCVPH to take also into account “recent scientific data from any source.” In fact, between 2000 and 2002, there had been a considerable number of new publications on relevant issues, including a first attempt for an assessment of the synthetic hormone melegenstrol acetate carried out by JECFA in 2000.

110. The SCVPH opinion, adopted at its plenary session on 10 April 2002 (hereinafter “the 2002 Opinion”), discussed in some detail the scientific developments and concluded that the validity of the two previous opinions was confirmed and that no amendments to those opinions were justified.

77 The US fails to mention these aspects in its First Written Submission, trying simply to impress the Panel with incomplete and misleading statements.
78 As already explained to the Panel, the 2005 UK draft report from the Veterinary Products Committee has already been sent by the European Commission to EFSA with the request to take it into account in its next review of these substances.
79 See Exhibit US – 17.
80 See the list of references attached to the 2002 Opinion.
81 See Exhibit US – 1. The SCVPH Committee received again the assistance of the specialised Working Group composed of 9 independent specialists, 4 of which are well known US scientists.
111. It is important to clarify here that the US advances, in its reply to Panel Question 49, a number of arguments for the proposition that the European Communities did not provide copies of its 2000 and 2002 risk assessments by the SCVPH to it. The United States reply to this question is based on an erroneous interpretation of the SPS Agreement and the DSU and the DSB recommendation in this case.

112. It should be stressed that a delegation of scientists that took part in the 1999 SCVPH opinion visited on 21 June 1999 the United States regulatory authorities and scientists. There were 11 scientists from the US side and 4 scientists from the European side, who replied to a long list of questions and explained in detail the 1999 opinion to their US counterparts. Before and after that meeting there was never any question by the United States representatives that they lacked the necessary documentation to study the 1999 SCVPH opinion. Equally, the 2000 and 2002 opinions of the SCVPH were made public shortly after their adoption and were easily accessible to all through the European Commission’s web-site. The United States now argues that the 2000 and 2002 risk assessments should have been followed by a meeting between the US and the European scientists similar to that of 1999. However, there is nothing in the WTO agreements to suggest such an obligation for an implementing party following panel proceedings. Moreover, in view of the dismissive attitude of the US authorities, which had questioned the validity of the SCVPH findings even before they had the time to study them, the atmosphere was not conducive for this kind of meetings between the scientists. Nevertheless, the issue of the ban on hormone treated meat and the DSB recommendation have been on the agenda of practically every bilateral meeting between the responsible European Commissioner for trade since 1998 with his USTR counterpart, and it is now totally unfounded for the US to argue that they have not received the relevant information concerning the 2000 and 2002 risk assessments. The truth is that the US regulatory authorities have never displayed any real interest to openly discuss the underlying scientific questions and accept scientific views different from those advanced by its own scientific bodies.
4. Risk assessment and risk analysis by the competent EC regulatory authorities

113. On the basis of the above scientific risk assessments provided by the SCVPH, the competent European regulatory authorities carried out an analysis of risk management options in light of the appropriate level of protection it had chosen.

114. In light of this, the European Communities arrived at the conclusion that it was necessary to maintain the permanent prohibition on oestradiol 17β and to continue to provisionally apply the prohibition to the other five hormones. Exceptions were made only for the use of certain of these substances for zootechnical and therapeutic purposes where no viable effective alternatives appeared to exist. This exception was based on the assessment that owing to the nature and limited duration of the treatments, the limited quantities administered and the strict conditions imposed to prevent misuse, made it that this use did not constitute a hazard for public health.

B. New scientific developments as reflected in the 1999 – 2002 SCVPH risk assessments

115. For purposes of providing some background to the ensuing legal debate, it seems useful to highlight the main issues that are at the centre of the scientific debate in these proceedings. In fact, there are a number of important scientific developments that have taken place over recent years which have impacted on the evaluations made of these hormones in a number of reports, also affecting the evaluation of possible risks from residues in meat treated with hormones for growth promotion.

1. The 1999 JECFA report on the three natural hormones

116. Both the United States and Canada make several references to the 1999 JECFA report on the three natural hormones (oestradiol 17β, testosterone and progesterone), without however mentioning the important qualitative differences in the findings of the 1999 report compared to its 1988 report.
117. There are many developments since the 1988 JECFA report, a few of which will be mentioned here. As regards the **carcinogenicity** of the three natural hormones, the 1988 JECFA report did not consider it necessary to set an ADI (acceptable daily intake) on the ground that these hormones are “produced endogenously in human beings and show great variation in levels according to age and sex”. The Committee concluded that residues arising from the use of these hormones as growth promoters in accordance with good animal husbandry practice are unlikely to pose a hazard to human health.

118. However, in the 1999 report, JECFA concluded that oestradiol “has genotoxic potential”, that progesterone “on balance has no genotoxic potential” and that testosterone “has no genotoxic potential”. Unlike in the 1988 report, however, JECFA proposed in 1999 to set an ADI for oestradiol 17β of 0-50 ng/kg/bw with a safety factor of 10; for progesterone an ADI of 0-30 mg/kg/bw with a safety factor of 100; and for testosterone an ADI of 0-2 mg/kg/bw with a safety factor of 1000.

119. The above are important developments. They confirm, at least for oestradiol 17β, what the European Communities has been arguing during the 1996 panel proceedings in the *Hormones* case, namely that these hormones are carcinogenic/genotoxic, although JECFA admits it now only for oestradiol 17β and denies it “on balance” for progesterone. JECFA now sees the need to set an ADI, but did not see that need in 1988. This means that exposure to residue intake of these hormones from any other source should not lead to levels exceeding the above ADI, a requirement JECFA did not consider necessary in 1988. More importantly, since the administration of hormones for animal growth promotion gives rise to residues in meat which, when consumed, add further to the exposure burden of humans, the European Communities’ level of protection aims to avoid this additional and unnecessary risk. So, the Codex/JECFA recommendations are

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82 The 1999 and 2002 risk assessments by the SCVPH arrived at the conclusion that: “In summary, additional and conclusive data have now been published in the scientific literature to demonstrate that 17β oestradiol is genotoxic. 17β oestradiol induces mutations in various cultured mammalian cells. The reactive metabolite, oestradiol-3,4-quinone, also induces mutations in mouse skin in vivo. The catechol oestrogen-quinones form DNA adducts in cultured cells and in mouse skin.” Moreover, it should be further clarified that it is generally recognised that for substances which have genotoxic potential (as is the case with oestradiol 17β) the low dose used in animal growth promotion is not relevant, precisely because the possible genotoxic risks may arise at any dose. So, there cannot be said to exist a safe threshold below which intake from residues in meat should be considered to be safe.
not only old but also do not allow the European Communities to achieve the level of protection it considers appropriate on its territory.

120. It is also important to recall that the 1999 JECFA report based its findings on residues data that are outdated by now. As already explained, the European Communities requested specifically Codex/JECFA to postpone its risk assessment until the findings from the new studies launched by the Communities became available, but Codex declined to do so. As already stated, the residues data used by JECFA in its 1999 report are not new. They come from the same old studies that were used also in the 1988 JECFA report, some of which are even “undated” and most of which are never published in peer-reviewed scientific journals. What is even more important, however, is that the toxicological findings in the 1999 JECFA report (as well as in its 1988 report) are not based on evidence from residues in meat from animals treated with these hormones for growth promotion purposes. JECFA makes extensive references to studies with experimental animals in vitro and in vivo and it refers also to the general studies of the International Agency for Research on Cancer (IARC).

121. Another recent development not taken into account by the 1999 JECFA report concerns the endogenous production levels of these hormones by pre-pubertal children. The 1999 SCVPH report found that:
The hormone levels presented above (Table 1) were determined by radio-immunoassays (RIA). Use of these assays has frequently been associated with production of variable results, particularly when used to detect low levels of endogenous hormones (Carlstrom, 1996; Potischman et al., 1994, Klein et al., 1994; documents prepared for the EC by Andersson and Skakkebaek, February 1999). Klein et al. (1994) developed and carefully characterized an ultrasensitive assay (100 fold more sensitive than RIAs) consisting of yeast cells genetically engineered to express the oestrogen receptor and a reporter gene under the control of a tandem repeat of the vitellogenin oestrogen response element. This assay is highly specific for detection of oestradiol. Using this assay Klein et al. (1994) report detecting serum oestrogen concentrations of 0.6 pg/ml and 0.08 pg/ml in prepubertal girls (n = 21, 7.7 years old) and prepubertal boys (n = 23, 9.4 years old), respectively. These values are considerably lower than the range of oestradiol levels shown in Table 1 that are typically reported for female (8-23 pg/ml) and male (5-14 pg/ml) prepubertal children. A corollary is that perhaps the hormone residues in beef, which are also low and which have also been determined by RIA are equally variable and over representative of the actual hormone concentrations. This is a critical area requiring additional study.

(at page 29, point 3.2)

122. The above findings establish that the levels of endogenous production of these hormones by pre-pubertal children is much lower than previously thought and this finding, which is subsequent to the 1999 JECFA report, casts serious doubts about the validity of JECFA’s findings on the dose-response relationship, because the data on endogenous production on which JECFA based its findings are also very old (since 1974). Thus, the 1999 SCVPH report found that:

In the USA, the FDA has established an acceptable level of exposure for oestradiol (Table 3). These values represent parent hormone residue levels in uncooked meat that are considered unlikely to produce any physiological effects in individuals chronically ingesting animal tissues.

Table 3: Acceptable levels of oestradiol levels in beef (Ref.: Code of Federal Regulations (CFR) 21, Part 556, Tolerances for residues of new animals drugs in food)

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Oestradiol (ng/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>120</td>
</tr>
<tr>
<td>Liver</td>
<td>240</td>
</tr>
<tr>
<td>Kidney</td>
<td>360</td>
</tr>
<tr>
<td>Fat</td>
<td>480</td>
</tr>
</tbody>
</table>
The FDA guidelines state that: "...no physiological effect will occur in individuals chronically ingesting animal tissues that contain an increase of endogenous steroid equal to 1% or less of the amount in micrograms produced by daily synthesis in the segment of the population with the lowest daily production. In the case of oestradiol and progesterone, prepubertal boys synthesize the least, in the case of testosterone, prepubertal girls synthesize the least" (taken from Andersson and Skakkebaek, 1999). The convention used by JECFA as the basis for determination of daily consumption of hormones is based on eating 500 g of meat per day (300g muscle, 100g liver, 50g kidney and 50 g fat). Based on this and the acceptable oestradiol levels in beef shown in Table 3, total daily consumption of currently acceptable levels of oestradiol would be 102 ng. This value represents approximately 1-2% of the currently used calculated daily production rates for oestradiol in prepubescent children.

As mentioned previously in the Exposure Considerations Section, the daily production rate for oestradiol was estimated to be 6 µg/day oestradiol in boys. These daily production rate (PR) values are determined by the formula:

\[
PR (\mu g/day) = \text{plasma concentration (\mu g/ml)} \times \text{metabolic clearance rate (MCR, ml/day)}
\]

However, there are two potential problems with these values. First, as mentioned previously (Exposure Considerations Section), determination of plasma concentrations of oestradiol is subject to considerable variability, relative insensitivity given its low levels in children, and interference. A new, highly specific, more sensitive assay for oestradiol indicated that blood oestradiol levels in girls may be as much a 13 fold less and in boys 100 fold less than previous determinations using RIAs indicate. Second, it does not appear that MCRs have ever been determined directly in children. Rather, it appears as if MCR values from adult women were used in the calculations of the PRs for children (Anderson and Skakkebaek, 1999). This approach may or may not be valid given the known differences in levels of SHBG (higher in children, which would reduce clearance), and likely differences in uptake and metabolism, etc. Given these issues, it is possible that the safety margin for oestradiol exposure used by the FDA may be in error and that acceptable levels of hormone residues in beef could be much lower. (Similar concerns apply to progesterone and testosterone).

The median level of excess exposure to oestradiol from consuming meat from hormone-treated cattle is 6.8 ng/person/day (calculated from Table A3, Annex, range 1 to 84 ng/person/day). For comparative purposes, assuming 100% absorption and a whole blood volume of 78ml/kg body weight, for a 40 kg child, based on the median value for excess oestrogen exposure, the blood concentration calculates to be 2.2 pg/ml (1 to 26 pg/ml).
If the blood oestrogen levels are 100 fold lower than previously determined and the MCR too high by a factor of 10, the oestradiol daily production rate could be as low as 6 ng, and 1% of this would be 60pg. Thus, the FDAs acceptable daily intake (102 ng/person/day, see above) could exceed the daily production rate of oestradiol by 1,700 fold. While there is some experimental evidence in support of the currently used blood levels of oestradiol being 100 fold too high (Klein et al., 1994), the other assumptions used in coming to this conclusion may be too conservative. Thus, if absorption is reduced to 10% and the MCR for children is only 1/2 that of adults, the FDA acceptable daily intake could still be 85 fold too high. Given all of the uncertainties in these estimates, it appears that the data are insufficient to form the basis of a sound risk assessment. Clearly, this is an important area for additional research.” (at pages 37-38, point 4.1.5.).

123. Another area where recent developments put in doubt the findings of the 1999 JECFA report concerns the bioavailability of residues of these hormones. The 1999 and 2002 SCVPH reports have found that data on which JECFA based its findings are incorrect or insufficient:

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83 Similar specific findings about risks to human health from residues in meat from animals treated with hormones for growth promotion have been made in the 1999 SCVPH report also for the other hormones. See points 4.2.4 for testosterone, 4.3.4. for progesterone, 4.4.4. for trenbolone acetate, 4.5.4. for zeranol, and 4.6.4. for melegestrol acetate.
At its February, 1999 meeting, JECFA established the ADI for 17β-oestradiol as 0-50 ng/kg bw/day. This value is based on a study in postmenopausal women where conjugated equine oestrogens at doses of 0.3, 0.62, 1.2 and 2.5 mg were administered for two weeks followed by no treatment for three weeks. This regimen was repeated four times after which serum levels of corticosteroid binding protein (CBG) were determined. No increase in CBG levels was detected at the 0.3 mg dose (equivalent to 5 µg/kg bw/day) which was thus considered to represent the no-observed-effect level (NOEL). In another analysis (it is not clear if this was part of the same study or a different one), the dose of 0.3 mg of conjugated equine oestrogen was determined to be the NOEL for induction of serum concentrations of follicle-stimulating hormone, angiotensinogen, SHBG and CBG. It was stated that fine-particle 17β-oestradiol and the conjugated equine oestrogens were equipotent for all four hormone-dependent end points. In a separate study, the bioavailability of fine-particle 17β-oestradiol administered orally was determined to be 5% compared to a dose administered intravenously. Sixty percent of the fine-particle 17β-oestradiol dose was determined to appear in the serum as estrone and estrone sulfate. While the results of these studies would appear to indicate that the maximum excess exposure level (84 ng/person/day) for oestrogen derived from hormone-treated beef is below the NOEL, there are several concerns. First, neither the actual data nor references to peer-reviewed publication of this data were available. Second, it is uncertain whether the use of fine-particle 17β-oestradiol, and in particular conjugated equine oestrogens, represents appropriate surrogates for consumption of oestrogens in association with beef. The equine oestrogens consist predominately of equilin and equilenin, which are chemically different from oestradiol.” (at pages 36-37, point 4.1.5).

124. Furthermore, the 2002 SCVPH report further clarified that:

4.1.5. Oestrogenic potencies of residues

In consideration of the studies of the metabolism of oestradiol, 17_–E2 and its metabolites were evaluated with regard to their oestrogenic activity in a traditional in vivo assay (uterotrophic effect in rats following oral administration)(study 3).
The obtained results indicate that the potency of 17_-E2 is approximately 10% of 17_-E2. However, the potency of the lipoidal esters exceeded the effect of 17_-E2 in the in vivo assay by approximately a factor of 10 (Paris et al., 2001). Furthermore, lipoidal esters appear to have an even higher effect on the mammary gland in experimental animals (Mills et al., 2001). The high potency of lipoidal esters after oral applications might be explained by the fact that they reach systemic circulation via the lymphatic system, as suggested by preliminary data. These findings warrant further investigation, as a high bioavailability of biologically active lipoidal esters and the possibility of accumulation (Larner et al., 1985) might contribute significantly to an undesirable exposure to oestrogenic substances. The impact of residual protein bound non-extractable oestrogen remains to be elucidated.

In conclusion, it has to be stated that lipoidal esters of oestradiol add to the oestrogen exposure, as mentioned above. While the oral bioavailability of these metabolites was high in animal experiments, no information is available on the oral bioavailability in humans following dietary exposure via contaminated meat products.” (at page 12, point 4.1.5. of the 2002 opinion).

2. Risks resulting from the possibilities of misuse or abuse when the administration of these hormones is freely authorised

125. Another very important area of research which all JECFA reports failed to address is the possibilities for misuse or abuse when the administration of these hormones is freely authorised “over the counter”, as is the situation in the United States and Canada. The 1999 SCVPH report has made important findings in this respect, which are summarised as follows:

The guidelines for implantation in cattle of growth promoting hormones are set by the requirements of Good Veterinary Practice, however, in most countries hormone containing implants are available "over the counter". Given this widespread availability of the implants and the incentive provided by the enhanced growth and feed utilisation efficiency resulting from hormone use, it is likely that some degree of misuse will occur. Types of misuse possible include improper placement of the implants (i.e. in tissue used for consumption rather than in the ears which should be discarded), off-label use, including use in non-approved animals (e.g. veal calves and pigs), overdosing, disease treatment, and use of black-market non-approved hormones. Each of these possibilities for misuse could result in over exposure of humans consuming beef from the affected cattle.
Misplaced implants

It is generally appreciated that the highest concentration of hormone residues will be at the implantation sites. In a study of the residues of TBA, zeranol, and DES remaining in the ears of cattle at slaughter, from 6% to 30% of the original dose remained in the ears from 65 to 150 days after implantation. The range of hormone amounts was approximately 6 to 54 mg even after these prolonged “withdrawal” times. These data indicate that consumption of tissue from implantation sites would result in substantial excess exposure. Model calculations provide estimates of the extent of excess exposure that could result from consumption of meat containing implantation sites.

Off-label use

Off-label use includes use of implants and feed premixes in species for which they were not approved. For example, use of growth promoting hormones in veal calves is not approved in the US or Canada. However, the Canadian Food Inspection Agency, in two surveys to evaluate misuse of TBA in veal calves uncovered violations. In one (1987), 33% of 281 samples and in the second (1997-98), 40% of 210 samples of liver from veal calves revealed the presence of TBA residues.

Furthermore, preliminary results from a study commissioned by the EC intended to determine the amount of hormone residues in US meat and offal samples detected the presence of off-label synthetic hormonal growth promoters in calf liver (Stephany and André, First Interim Report, 1999).

In an ongoing EC commissioned study of hormone residues in edible tissue from beef of cattle designated to be hormone-free from the USA, measurable levels of trenbolone, zeranol and melengestrol were detected in approximately 12% of 258 samples of bovine meat (Stephany and André 1999, interim report). Various examples of overdosing by simultaneous and/or repeated implantation of various implants in USA feedlots have also been documented by EC inspection missions (Draft Report, 1999, see above).

Finally, hormones might be used in other species including pigs and poultry. The potential residue burden originating from these illegal treatments are currently under investigation. In these studies, the stability of hormones and their metabolites in manure and the possible risk to the environment will be addressed as well.

Black-market drugs

The possibility that non-authorized pharmaceutical formulations of hormones will be used in animals can not be excluded. These black-market drugs may comprise an even higher risk to public health, as their quality is often inadequate.
Finally, misplaced implants and/or illegal drugs may impair animal health and welfare and animal husbandry (due to induction of behavioral abnormalities). These possible effects to animals’ health and welfare have not been discussed in detail, as this report is focussing on public health.

**Secondary risks**

It is well recognized that the expression of drug-metabolizing enzymes (DMEs) is regulated by hormones and sex differences in the disposition and metabolism of veterinary drugs have been described in various animal species, including ruminants (Witkamp et al., 1991, Witkamp et al., 1993a and b, van't Klooster et al., 1993, Motesissa et al., 1996). More specifically, the effect of trenbolone and testosterone on the plasma elimination rate of different veterinary drugs, including sulfamethazine and trimethoprim were studied in goats. It could be demonstrated that these anabolic steroids prolong the elimination rate of drugs (van Miert et al., 1988). In consideration of these findings it has to be assumed that the use of hormones for growth promoting purposes will increase the prevalence of undesirable residues (in particular of antibiotics which are frequently used in bovine therapy) in edible tissues of treated animals.

In conclusion, it has to be noted that misplaced implants and black market drugs comprise the risk that extremely high levels of residues of hormones remain in edible tissues of animals. In addition, it has to be noted that the contemporaneous use of growth promoting hormones and veterinary therapeutics drugs increases the prevalence of undesirable residues in edible tissues of bovines.” (pages 30-32, point 3.3. of 1999 SCVPH report).

126. The above findings are based on realistic conditions of use and the possibilities of abuse or misuse which these hormones offer to farmers and are documented – as regards the United States and Canadian markets - in the attached assessment report. Moreover, as it will be explained further below, concrete examples of misuse and the risks this presents for human health are provided from the United States and Canada, following inter alia veterinary inspections that were carried out there by European Commission officials. Abuses or misuses of these hormones, which are sold freely “over the counter” in the defending parties, are

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84 See Working Document: Assessment of risks of hormonal growth promoters in cattle with respect to risks arising from abusive use and difficulties of control, prepared by a special working group of external private experts and European Commission officials, 29 April 1999, Exhibit EC - 18.

85 See EC – Exhibit 12 and Exhibit EC - 13. These reports were cited in the EC Reply to Panel Question 31, para. 171.
not uncommon as it can be seen from the evidence attached hereto, showing illegal use in 2003-2005 of unapproved growth hormone implants in veal calves in the US, and extra label use in Canada.

127. The above are some of the most important scientific developments that have occurred before or just after the 1999 and 2000 findings of JECFA and which invalidate or put into serious doubts the relevance and sufficiency of evidence on which its reports are based. The European Communities will revert to these and some other seminal scientific developments subsequently in this rebuttal.

III. legal arguments

A. Burden of proof

128. The United States’ arguments on burden of proof are actually confused as they do not distinguish between arguments in Part I (violation of the DSU irrespective of the question of actual compliance) and arguments in Part II (violation claim based on actual compliance) of the EC First Written Submission. In particular, the United States speaks of “bald assertions” on compliance and it is not clear whether the alleged boldness lies in the argument that there is a presumption of compliance (Part I) or in the presentation of facts on the comprehensive risk assessment (Part II).

129. To the extent the latter is meant, the European Communities, at the oral hearing and in reply to the Panel’s questions, has already taken a position on the question of its burden of proof for demonstrating a violation of Articles I:1 and II of the GATT 1994 and that the measure found to be inconsistent has been “removed” in the context of a direct claim under Article 22.8. In particular, the European Communities has pointed out that it cannot be required to prove a negative, namely that there is no violation of WTO obligations. Indeed, in line with the established case law of the Appellate Body, it is for the United States and Canada,
in this case, to set out a *prima facie* case of violation, and not for the European Communities to set out a case of non violation.

130. The extent of what the European Communities has to demonstrate when arguing that the measure has been “removed”, therefore, cannot go beyond setting out what it has effectively set out in its First Written Submission. It has described there the new measure and has explained that that measure is now in compliance with the rulings and recommendations of the DSB in the *Hormones* case, as it is based on a comprehensive risk assessment. It has outlined the main conclusions of this risk assessment and has put a reference to the online texts of the scientific opinions underlying that risk assessment.

131. It is for the defending parties to rebut this *prima facie* case of compliance in putting forward arguments as to why there is no compliance. They have tried to do so and the European Communities, in the following sections, will rebut the arguments they have put forward.

B. *The provisional bans on five of the hormonal substances do not violate Article 5.7*

132. The United States argues that the provisional bans on the five hormonal substances progesterone, testosterone, trenbolone, zeranol and MGA are in violation of Article 5.7 of the *SPS Agreement*. The main argument of the defending parties is that the scientific evidence on these substances is not “insufficient” within the meaning of Article 5.7. However, the United States also argues that others of the four requirements of Article 5.7 are not fulfilled. The European Communities, in the following sections, will address these arguments one by one.87

1. **Relevant scientific evidence is insufficient**

87 There is a disagreement between the parties as to the nature of Article 5.7. In the defending parties’ view that provision is an exception to Article 2.2, in the European Communities’ view it is a special regime in relation to Article 5.1 (see EC Replies to Panel Questions 66, paras. 242ff). For the purposes of this case, and in particular the question of burden of proof, the question can actually be left open as the defending parties, in this particular constellation, have anyway the burden of proof of demonstrating that Article 5.7 has been violated.
133. The United States argues that the provisional bans are incompatible with Article 5.7 of the SPS Agreement because the relevant scientific evidence would not be “insufficient”. The United States claims that there is more than sufficient scientific evidence relating to the five hormones to permit adequate assessment of any potential risks, referring in particular to the JECFA 1999-2000 reports and the CVMP report of 1999.88

134. As the United States rightly recalls, relevant scientific evidence is insufficient, according to the Appellate Body in the case Japan – Apples,

> if the body of available scientific evidence does not allow, in qualitative or quantitative terms, the performance of an adequate assessment of risks as required under Article 5.1 and as defined in Annex A to the SPS Agreement.89

135. The United States further refined its views on the (non) application of Article 5.7 of the SPS Agreement in this case with its replies to Questions 67-73 of the Panel. It is important to note, however, that the US admitted there that:

> While the United States believes that there can be situations in which there is insufficient scientific information for a Member to perform a risk assessment even when an international standard exists, the simple fact in this dispute is that international standards and a significant body of scientific studies exist on the risks posed by the five hormones. It would therefore be very difficult to demonstrate that the relevant conditions of Article 5.7 have been satisfied, e.g., that there is insufficient scientific evidence concerning the hormones.

> Although it is not the case here (see U.S. answer to Panel question 69), it is possible that, if scientific evidence is sufficient to conduct a proper risk assessment at one point in time, it will later be insufficient to conduct such an assessment. Such a situation might arise, for example, when evidence of a new pathway for a risk comes to light, but the data concerning that pathway, while sufficient to identify it, is not adequate to perform a risk assessment. International standards serve as an indicator that evidence is sufficient to conduct a risk assessment.90

136. The European Communities considers that, in light also of this statement, the conclusions to which the SCVPH came on the basis of the data available on

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89 Appellate Body Report, Japan – Apples, para. 179.
90 See US Replies to Questions 72 and 73, paras. 81 and 82, emphasis added.
progesterone, testosterone, zeranol, trenbolone acetate and MGA are fully justified.

137. The United States’ main argument against this conclusion seems to be that the European Communities, back in 1996, when arguing the case before the Hormones panel, had itself stated that it considered the evidence to be sufficient. This point has already extensively been discussed at the first substantive hearing, in the replies to the Panel’s questions, and earlier in the present submission. The European Communities will, therefore, limit itself to recalling that: (1) what the European Communities had considered to be sufficient evidence had been found to be insufficient by the Appellate Body and proved indeed to be insufficient also in the light of risk assessment standards that were developed in the years after the Hormones decision; and (2) the body of evidence, in the meantime, has developed and, while still not providing enough knowledge to carry out a complete and definitive risk assessment, supports the conclusion that precautionary measures are required in order to achieve its chosen level of protection.

138. In the following paragraphs, therefore, it will be briefly explained with regard to each of the five hormonal substances in question, what this body of evidence consists of and why it provides a rational basis to the EC’s compliance measure.

139. As will be seen, the evidence, while pointing to a number of risks, is full of gaps in pertinent information and important contradictions have developed that render no longer valid the conclusions reached by JECFA in 1988, 1999 and 2000. Thus, it does not allow in qualitative or quantitative terms, the performance of an adequate assessment of risks as required under Article 5.1 and as defined in Annex A to the SPS Agreement.

140. The defending parties, apart from simply asserting that these substances have been intensively studied over the last twenty five years, do not put forward much if any substantive arguments to demonstrate why the above evidence assessed by the SCVHP, also in the light of the latest scientific developments and the results of the

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91 See in particular, EC Replies to Questions 19, 67 and 73.
92 See also Executive Summary and answers to the questions in the mandate in SCVHP Opinions of 1999 and 2002.
specific 17 studies, would not be insufficient to apply Article 5.7 SPS. They hide behind outdated evaluations made by JECFA and the criticism made by the Canadian, UK and Australian authorities of the new risk assessment carried out by the SCVPH.

141. Moreover, they repeat arguments and make reference to evidence that was found by the Appellate Body to be either irrelevant (such as the whole discussion about naturally occurring hormone residues in food and the December 1999 CVMP report and the arguments about therapeutic or zootechnical use) or inappropriate. It is important to recall what the Appellate Body stated in this regard:

We do not share the Panel's conclusions that the above differences in levels of protection in respect of added hormones in treated meat and in respect of naturally-occurring hormones in food, are merely arbitrary and unjustifiable. To the contrary, we consider there is a fundamental distinction between added hormones (natural or synthetic) and naturally-occurring hormones in meat and other foods. In respect of the latter, the European Communities simply takes no regulatory action; to require it to prohibit totally the production and consumption of such foods or to limit the residues of naturally-occurring hormones in food, entails such a comprehensive and massive governmental intervention in nature and in the ordinary lives of people as to reduce the comparison itself to an absurdity. The other considerations cited by the Panel, whether taken separately or grouped together, do not justify the Panel's finding of arbitrariness in the difference in the level of protection between added hormones for growth promotion and naturally-occurring hormones in meat and other foods.

142. It should be noted that in its reply to Question 67 of the Panel, the United States points out that for the purposes of establishing sufficiency (or insufficiency):

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93 US First Written Submission, at para. 125; see also US Replies to Panel Questions, at paras. 68 and 70 (the latter contains a footnote which, other than referring to JECFA, refers to the assessment of oestradiol 17β, which is not relevant here).

94 Appellate Body Report, EC- Hormones, at para. 221, footnote omitted. As regards possible inconsistency in the treatment of risks associated with therapeutic or zootechnical use, the Appellate Body found that: “The conclusion we come to, after consideration of the foregoing factors, is that, on balance, the difference in the levels of protection concerning hormones used for growth promotion purposes, on the one hand, and concerning hormones used for therapeutic and zootechnical purposes, on the other, is not, in itself, "arbitrary or unjustifiable." (at para. 225).
[T]he relevant question is not the specificity of the evidence relating to the five hormones, but rather whether all the evidence relating to those hormones, in toto, permits the EC to conduct a risk assessment for those hormones.  

143. The European Communities has pointed with its written and oral submissions and the replies to written questions from the Panel to a number of significant scientific developments which, taken together with all other available evidence, indicate that it is not possible to undertake a definitive risk assessment for these five hormones, within the meaning of Article 5.7 of the SPS Agreement. The 1999-2002 opinions of the SCVPH clarified the new scientific developments, identified the areas of scientific uncertainty and pointed to the important gaps in the general knowledge about the risks which residues in meat of these hormones pose to human health. The most important of these have been highlighted in the European Communities’ replies to the written questions as well as in the previous sections of this submission concerning the carcinogenicity, genotoxicity, dose-response and lack of safe thresholds, endogenous production by pre-pubertal children, lack of reliable bioavailability data, possibilities of abuse and lack of control, etc., and will not be repeated here again.

144. What is important to note is that, since the latest risk assessment by the SCVPH in 2002, there appeared internationally a number of further scientific developments all of which diverge toward, and provide further support to, the conclusions reached by the relevant scientific committee of the European Communities.

145. Namely, a group of independent US scientists has recently published in a peer-reviewed scientific journal evidence concerning zeranol (and oestradiol 17β) stating that:

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95 US Replies to Panel Questions, at para. 67.
Zeranol (Ralgro) is a nonsteroidal agent with estrogenic activity that is used as a growth promoter in the U.S. beef and veal industry. Thus zeranol is not an environmental contaminant per se. Rather, people are exposed to zeranol 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 zeranol-implanted cattle possess heat-stable mitogenicity for cultured breast cells, and that both normal and cancerous human breast cells exhibit estrogenic responses to zeranol (6-8). Evidence indicates potential tumorigenic mechanisms for estrogen, such as direct genotoxic effects of estrogen metabolites and estrogen-induced expression of genes encoding growth and transcription factors. However, despite the clear importance of estrogens in the etiology of breast cancer, the mechanisms responsible for estrogen-stimulated carcinogenesis remain undefined.96

146. The research for this study was supported by the Ohio State University, the US National Cancer Institute and the US Department of Defence Breast Cancer Research program. The European Communities would expect that the USA competent authorities will take the necessary steps to try and clarify the issues raised in this study and that other cautious WTO members would be entitled to take into account this kind of new pertinent evidence.

147. Furthermore, in June 2005 were published the results of a very large scale epidemiological study in Europe suggesting that high red meat intake is associated with (statistically significant) increased colorectal cancer risk, confirming results from previous smaller studies.97 The findings of this study are important in view of its very large scale, and they further reinforce the findings made in section 2.3.2.1. of the 1999 SCVPH opinion.

148. In 2002 were published the results from the women’s health Initiative Randomised Controlled Trial findings indicating that the risks outweigh the benefits from the use of oestrogen plus progestin in healthy postmenopausal


97 See Teresa Norat et al.: Meat, Fish, and Colocteral Cancer Risk – the European prospective investigation into cancer and nutrition, 97 Journal of the National Cancer Institute, p. 906-916 (15 June 2005); attached as Exhibit EC-16. The study was carried out after the introduction of the ban on the use of hormones for growth promotion in Europe, which means that the subjects should have been exposed to hormone-free meat in their diet. This may further imply that it cannot be excluded that the risk of cancer may be further increased if meat treated with hormones for animal growth promotion were to be consumed.
women, thus reinforcing the previous findings made by the IARC in this respect.\textsuperscript{98} They also reinforce the findings made in section 2.3.2.2. of the 1999 SCVPH opinion.

149. The more general point the European Communities would like to make at this stage is that the overall evidence and most recent scientific developments have now clearly tipped the balance against the previously held assumption (by the defending parties and Codex/JECFA) that residues of these hormones in meat from animals treated for growth promotion pose no risk to human health. There is now clearly no basis to suggest that the evidence which served as the basis in the 1988 and 1999-2000 JECFA evaluations of these hormones is sufficient to perform a definitive risk assessment within the meaning of Article 5.7 of the \textit{SPS Agreement}, in particular by the WTO Members applying a high level of health protection of no risk from exposure to unnecessary additional residues in meat of animals treated with hormones for growth promotion. To deny the existence of this new scientific reality would be to deprive the European Communities and other WTO Members of their autonomous right to choose their appropriate level of protection, because it would in effect impose on them a requirement to demonstrate positively the existence of clear harm, which they may not always be able to fulfil in case of cancer because of the long latency period and the numerous confounding factor that play a role. This will render the application of Article 5.7 impossible in a situation where the body of the pertinent scientific evidence is in the process of moving from a state of presumed “sufficiency” into a state of pertinent “insufficiency”. The text and preparatory history of the \textit{SPS Agreement} do not support such a (restrictive) construction of Article 5.7, which would moreover be against the principle of effective treaty interpretation.

150. To shed further light on this crucial issue, the European Communities would like to discuss the example of \textit{carbadox}, an antibacterial drug used to promote the growth of pigs. The 1997 panel reports in the \textit{Hormones} dispute found that the EC was in breach of its obligations under Article 5.5 of the \textit{SPS Agreement} because it

allowed the use of carbadox whilst it prohibited the use of hormones.\(^\text{99}\) However, the Appellate Body reversed this finding on the grounds that the difference in the levels of protection did not result in a discrimination or disguised restriction on trade.\(^\text{100}\) The important point to note is that the European Communities had already initiated the internal procedures to withdraw the authorisation for Carbadox on the basis of earlier scientific reports suggesting that its residues were genotoxic. And indeed, shortly after the panel reports were out it prohibited the use of Carbadox in the European Community in order to achieve its very high level of protection.\(^\text{101}\) But unlike the EU, the US and Canada continued to authorise the use of carbadox on the basis of a 1990 JECFA report which, while acknowledging the genotoxic nature of carbadox (with the consequence that ADI was fixed), did recommend MRLs on the ground that they were not exceeded in the residues data available. In 2003, JECFA produced a new evaluation of carbadox on the basis of some new evidence and decided to withdraw the MRLs recommended in 1991.\(^\text{102}\) As of today, more than five years after the EC prohibited the use of carbadox in its territory on the basis of the early evidence available, the defending parties still adopt different positions in Codex. It appears that the US is still arguing that the MRL for carbadox should remain in place, whereas Canada is now in favour of their abolition.

151. The case of carbadox is a clear example of a situation where the state of pertinent scientific information has moved (in a space of about ten years) from “sufficient” to authorise Carbadox in 1991 to a state of “sufficient” to prohibit it in 2003, and the Codex Commission has decided in 2005 to withdraw the MRL previously recommended. In 1998, however, when the European Communities decided to withdraw the authorisation for carbadox, the state of the pertinent scientific information was in the process of moving from the previously presumed “sufficiency” to authorise carbadox into a state of presumed “insufficiency” to continue with its authorisation. In other words, there is always a certain state of


\(^{100}\) See WT/DS26/AB/R and WT/DS48/AB/R, para. 246.


flux in the period between the evolution of the pertinent scientific information from “sufficient” to “insufficient”. It is submitted that during that period of uncertainty no WTO Member, applying a high level of protection should suffer if it decides to have recourse to Article 5.7 of the *SPS Agreement*.

152. The European Communities considers that the example of the evolution of the state of scientific evidence in carbadox is, *ceteris paribus*, comparable to the evolution of the body of evidence in the case of these hormones. Indeed, the EC is confident that it will be not before long that the defending parties and Codex/JECFA will have to face sincerely the new scientific developments and propose the withdrawal of these hormones for animal growth promotion in their territories because they are clearly dangerous to human health, animal health and the environment.103

2. Brief description of insufficiency of pertinent scientific information for all five hormones (except oestradiol 17β)

153. Before explaining more precisely some of the basic reasons for which the SCVPH found the evidence insufficient to complete or to carry out a definitive risk assessment, within the meaning of Article 5.7 of the *SPS Agreement*, it seems useful to provide here the summary of its findings for all five hormones which are subject to the provisional ban. In its 1999 report the SCVPH found that:

With the exception of 17-β oestradiol, the currently available information for testosterone, progesterone and the synthetic hormones zeranol, trenbolone and particularly MGA has been considered inadequate to complete an assessment. This conclusion is based upon:

– incomplete data on the biotranformation pathways of these compounds and the possible biological activity of the metabolites formed in bovine tissues as, for example, testosterone might be aromatized to oestradiol.

lack of data on the potential genotoxicity of these metabolites in consideration of the current state of the art for genotoxicity testing as indicated in the answer to question 2 (a).

insufficient data on immunological and immunotoxical effects.

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103 As regards the numerous adverse effects on animal health and the environment, see the 2002 Opinion of the SCVPH, the studies submitted with the replies to the written questions of the Panel, and the 2005 report of the UK CVP.
Based on experimental and epidemiological data, testosterone and progesterone have been classified by IARC as Group 2 substances - probable/possible carcinogens in humans. No epidemiological data are available for zeranol, trenbolone and MGA (melengesterol acetate) although residues of hormonally active compounds in (poultry) meat have been shown to exert an oestrogenic response in prepubertal children in certain countries.

Thus, no final conclusions can be drawn with respect to the safety of at least five out of the six substances under consideration, until the above described issues have been clarified. For oestradiol genotoxicity has already been demonstrated explicitly."

Appropriate systems to test for potential carcinogenic and genotoxic effects are all cells, tissues or tissue cultures or any other model resembling bovine and human metabolism (pronounced species differences in biotransformation are well documented in the literature). This implies that a battery of tests is needed, first to establish bovine biotransformation of the compounds under consideration (usually bovine microsomes or bovine hepatocytes and, with respect to oestrogens, bovine cells/tissues expressing CYP1B1) and, secondly, in the assessment of human bioprocessing of the bovine metabolites, systems resembling human biotransformation reactions (generally microsomes, human cell lines or genetically engineered cells) carrying at the same time a reporter gene to assess genotoxic events. However, it should be noted that standard tests of genotoxicity are not appropriate as the lack of a response in these assays may be related to the use of liver extracts for enzymatic activation, since oestrogen 4-hydroxylase activity is low in this organ. Additionally, the reactive intermediates may not be able to travel into target cells, and the types of DNA damage assayed may not be sufficient. The genotoxicity of oestrogen metabolites may best be assayed in mammalian cells with appropriate biotransformation enzymes (for example the human breast epithelial MCF-7 cell line), and the DNA damage analysis should include not only point mutations and frameshift mutations, but also chromosomal damage.

If there is convincing evidence, as in the case of 17-ß oestradiol, that metabolites of a hormone are genotoxic the answer is no. In the present state of the art, compounds that are used intentionally in food production and food processing should not yield genotoxic residues because no threshold can be established for this toxicological effect.

In addition, no threshold level can be established for other effects as cited in the answer to question 1a.

Since risk assessment was based at that time on hormonal effects only and no excess exposure was envisaged, the genotoxic and carcinogenic potential of residues in meat and meat products was not considered.

However, in the 1999 report of JECFA, more recent work on biotransformation mediated genotoxicity was cited.

As detailed in the report presented here evidence is provided that for hormones, no threshold can be defined either for the endocrine, developmental, immunological and neurobiological effects or for their potential immunotoxicity and carcinogenicity. This statement is also made in the light of the emerging concerns of the effects of hormones at different stages of life and the accumulating epidemiological findings on tumor incidence as recently summarized by IARC." (at pages 75-77).
154. The above findings were further confirmed and clarified by the 2002 Opinion of the SCVPH, the general conclusions of which were the following:

The review of the 17 studies launched by the European Commission and a recent scientific literature allows the following conclusions:

- Ultra-sensitive methods to detect residues of hormones in animal tissues have become available, but need further validation.

- Studies on the metabolism of $17\_\text{-oestradiol}$ in bovine species indicate the formation of lipoidal esters, disposed particularly in body fat. These lipoidal esters show a high oral bioavailability in rodent experiments. Thus, the consequence of their consumption needs to be considered in a risk assessment.

- Experiments with heifers, one of the major target animal groups for the use of hormones, indicated a dose-dependent increase in residue levels of all hormones, particularly at the implantation sites. Misplaced implants and repeated implanting, which seem to occur frequently, represent a considerable risk that highly contaminated meats could enter the food chain. There is also a dosedependent increase in residue levels following the oral administration of melengestrol acetate at doses exceeding approved levels, with a corresponding increased risk that contaminated meats could enter the food chain.

- Convincing data have been published confirming the mutagenic and genotoxic potential of $17\_\text{-oestradiol}$ as a consequence of metabolic activation to reactive quinones. *In vitro* experiments indicated that oestrogenic compounds might alter the expression of an array of genes. Considering that endogenous oestrogens also exert these effects, the data highlight the diverse biological effects of this class of hormones.

- No new data regarding testosterone and progesterone relevant to bovine meat or meat products are available. However, it should be emphasized that these natural hormones are used only in combination with $17\_\text{-oestradiol}$ or other oestrogenic compounds in commercial preparations.

- Experiments with zeranol and trenbolone suggested a more complex oxidative metabolism than previously assumed. These data need further clarification as they might influence a risk assessment related to tissue residues of these compounds.

- Zeranol and trenbolone have been tested for their mutagenic and genotoxic potential in various systems with different endpoints. Both compounds exhibited only very weak effects.

- Data on the genotoxicity of melengestrol acetate indicate only weak effects. However, pro-apoptotic effects were noted in some cell-based assays, which were attributed to the impurities in commercial formulation. Further experiments should clarify the toxicological significance of these impurities.

- Model experiments with rabbits treated with zeranol, trenbolone or melengestrol acetate, mirroring their use in bovines, were designed to study the consequences of pre- and perinatal exposure to exogenous hormones. All compounds crossed the placental barrier easily and influenced to varying degrees the development of the foetus, at the doses used in the experiments.
Epidemiological studies with opposite-sexed twins, suggest that the exposure of the female co-twin *in utero* to hormones results in an increased birth weight and consequently an increased adult breast cancer risk.

- Several studies were devoted to the potential impact of the extensive use of hormones on the environment. Convincing data were presented indicating the high stability of trenbolone and melengestrol acetate in the environment, whereas preliminary data were provided on the potential detrimental effects of hormonal compounds in surface water.

*In conclusion*, after re-appraisal of the data from the 17 studies and recent scientific literature, the SCVPH confirms the validity of its previous Opinions (in 1999 and 2000) on the Assessment of Potential Risks to Human Health from Hormone Residues in Bovine Meat and Meat Products, and that no amendments to those opinions are justified.¹⁰⁴

(a) **Progesterone**

155. As regards progesterone, the SCVHP found *inter alia* the following insufficiencies in the evidence:

Little is known about the specific enzymes in cattle that metabolize progesterone, although hepatic cytochrome P450 enzymes are likely involved in the metabolic clearance of this hormone…

The tolerance levels for progesterone levels in uncooked tissues of steers and calves established by the FDA (Ref.: *Code of Federal Regulations (CFR) 21, Part 556, Tolerances for residues of new animals drugs in food*) are:

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Progesterone (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>3</td>
</tr>
<tr>
<td>Liver</td>
<td>6</td>
</tr>
<tr>
<td>Kidney</td>
<td>9</td>
</tr>
<tr>
<td>Fat</td>
<td>12</td>
</tr>
</tbody>
</table>

Based on these levels, consumption of 500 g/day of beef (300g muscle, 100g liver, 50g each of kidney and fat) would result in exposure to approximately 2.6 µg/person/day. This amount represents approximately 1-2% of the daily production rate for progesterone of 150 µg/day estimated for prepubertal boys, and approximately 0.3% of the maximum excess exposure to progesterone estimated to occur upon consumption of meat from hormone-treated cattle (Table A3, Annex). However, there is considerable uncertainty associated with the validity of the daily production rate data. It is possible that this value has been over estimated by one to two orders of magnitude, in which case excess progesterone intake from hormone-treated beef could at best exceed the 1% FDA safety margin and at worst be greater than that naturally present.

**Progesterone Levels in Human Blood:** The data show that premenopausal women have the highest levels of endogenous progesterone (Table 1, section 3.1). Progesterone production rates in premenopausal women during the follicular phase have been determined to be approximately 418 µg/day (JECFA, 1987 monograph). During pregnancy, progesterone production rates during late pregnancy have been determined to be approximately 94,000 ug/day (JECFA, 1987 monograph). In men, the daily production rate for progesterone is approximately 416 µg/day, respectively (JECFA, 1987). In prepubertal boys, the progesterone production rate has been reported to be 150 µg/day (JECFA, 1987). Thus, prepubertal and postmenopausal females and prepubertal and adult males have the lowest levels of endogenous progesterone and thus would represent the individuals most likely to be at increased risk for adverse health effects that might be associated with exposure to exogenous sources of oestrogens.

The toxicological issues of concern include endocrine, developmental, immunological, neurobiological, immunotoxic, genotoxic and carcinogenic effects. Specific hazardous effects are detailed below.

**Mutagenicity and genotoxicity of progesterone**

No information is available.

**DNA adducts and DNA damage**

No information is available, although the 1999 JEFCA report refers without data or reference to induction of single-strand DNA breaks and DNA adducts from in vivo and in vitro studies.

**Carcinogenicity**

Progesterone has been shown to increase the incidence of tumours in laboratory animals in the following target tissues: mammary gland, ovary, uterus and vagina (Jones and Bern, 1977; Frank, et al., 1979).
The evidence for carcinogenicity in humans is considered inadequate. Most of the human evidence on the effect of progesterone on cancer risk comes from studies on progestogen-only contraceptives, available for the last 20 years, either as progestogen–only mini-pills or intramuscular depot injections and subcutaneous implants. Studies have been conducted on breast, endometrial, cervical, ovarian and liver cancer, as well as cutaneous melanoma.

In conclusion, as the evidence is considered sufficient in experimental animals for the carcinogenicity of medroxyprogesterone acetate, (and inadequate for levorgestrel), the overall evaluation of IARC resulted in the allocation of progestogen-only contraceptives in group 2B, possibly carcinogenic to humans. At present the data are insufficient to make any quantitative estimate of the risk arising from the exposure to residues in meat and meat products originating from treated animals.

Effect of progesterone on growth and reproduction

Progesterone is the major progestogen secreted by the corpus luteum during the luteal phase of the ovarian cycle in women of adult age. Plasma levels of progesterone are low in men, in children and in women during the follicular phase of the ovarian cycle.

In physiological conditions, endogenous progesterone secreted by the ovary in the female exerts negative feedback effects on the secretion of the luteinizing hormone (LH), acting on the hypothalamo-pituitary system. During the luteal phase of the ovarian cycle, LH pulsatility is low and ovulation is prevented until the demise of the corpus luteum. Continuous administration of exogenous progesterone to an adult female leads to interruption of ovarian cycles and blocking of ovulation, when the doses administered allow to obtain plasma levels similar to those of a normal luteal phase. In cattle, implants delivering lower doses of progesterone corresponding to subluteal plasma levels induce an increase in LH pulsatility, the lengthening of the estrous cycle and the presence of large persistent follicles on ovaries (Stock and Fortune, 1993). In the male, alterations of spermatogenesis can be induced by progesterone treatments. No assessment of the dose response relationship has been presented yet.

Effects of progesterone on the immune system

A limited number of investigations have been made. Progesterone has been shown to reduce the ability of cows to combat bacteria introduced into the uterus (Rowson et al., 1963).

Progesterone when administered at high levels has also been shown to depress the production of antibodies to experimental infections of candida albicans. At low doses immuno stimulation was claimed (Malhur, et al., 1978)
In sheep progesterone was found to regulate immune function, resulting in its inhibition at the utero placental interface without systemic immuno suppression (Hansen, 1998).

In conclusion, these data indicate that progesterone can cause immuno depression; however, they are insufficient to make any realistic assessment of the dose response relationship.”

156. In addition, the SCVHP noted that currently Progesterone, when used for growth promotion purposes is only used in combination with oestradiol 17β, the genotoxic potential of which has been established.

157. In claiming that there is sufficient scientific evidence on this substance, the United States summarily refers to the 1999 assessment that had been carried out by JECFA. As a matter of fact, this assessment had been taken into account by the SCVHP. The SCVHP had found in particular (at pages 52-53) that:

At its February 1999 Meeting, the JECFA established for progesterone an ADI of 0-30 µg/kg bw (0-2,100 µg/70 kg person). This value was based on studies where a lowest-observed-effect level (LOEL) of 200 mg fine-particle progesterone (equivalent to 3.3 mg/kg bw) was determined and includes a safety factor of 100 to allow for extrapolation from the LOEL to a NOEL. In one study, designed to explore anti-proliferative and secretory endpoints in the endometrium, women were treated with 300 or 600 mg/day of fine-particle progesterone for two weeks following a thirty day pretreatment with oestrogen. The group treated with the 300 mg dose showed incomplete conversion of the uterus to full secretory activity whilst the group receiving the 600 mg dose did. In an additional studies using 200 or 300 mg oral doses of progesterone for one or five years, there was no evidence of endometrial hyperplasia or carcinoma. In addition, it was stated that a single oral dose of 200 mg fine-particle progesterone produced concentrations of progesterone in blood similar to those found during the luteal phase of the ovulatory cycle. While these data indicate that the daily exposure from consuming hormone-treated beef is well below the ADI, there is some concern regarding determination of the ADI. First, neither the actual data nor reference to a peer-reviewed publication was provided. Second, the dose-response was limited to two doses and the ADI was estimated from just a single dose rather than a curve derived from all the data available.

158. The United States only highlights one aspect of the JECFA assessment which is that it included “detailed epidemiological studies on the effects of the hormones on

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post-menopausal women, marking some of the most relevant studies of the effects of hormones on human beings to date.”¹⁰⁷ This reference, in the context of an assessment of progesterone is erroneous, in light of the most recent (2002) data cited above concerning the serious adverse effects observed in the study on post-menopausal women.

159. Equally erroneous is the United States’ reference to the CVMP’s opinion in this regard. As already explained, for the purposes of this dispute any reference made to the opinions of the CVMP are irrelevant. In any case, the CVMP’s assessment, which concerned the safety of progesterone when used for zootechnical and therapeutic purposes, pointed out that only few recent data were available for re-evaluation of the carcinogenic and/or genotoxic properties of progesterone had concluded that the compound (1) is not genotoxic in most of the tests performed and (2) increases tumor incidences in animals at exposure levels clearly above the physiological levels.¹⁰⁸

(b) Testosterone

160. As regards testosterone, the SCVHP found inter alia the following insufficiencies:

Androgen receptors are detected in tissues of females, as well as males. The presence of this receptor in organs such as the ovary indicates significant activity of androgens in both sexes. Furthermore, the androgen receptor is thought to be involved in ovarian tumorigenesis, as it has been detected in 67 percent of ovarian tumors. Although current information indicates the presence of only a single androgen receptor, it is known that different subsets of genes may be activated by either testosterone or DHT (Chang et al., 1995). Thus, as for other steroid hormone receptor pathways, the mechanism of androgen activity is only partially understood. It is also of importance to note that testosterone can be aromatized to oestradiol in tissues containing CYP450 aromatase (CYP19)…

¹⁰⁷ US First Written Submission, at para. 127.
¹⁰⁸ Exhibit US – 13, at p. 11.
Little information is available about the specific metabolic routes and elimination rates for testosterone in cattle. In rats, seven pathways of testosterone oxidation, $2\alpha$, $2\beta$, $6\beta$, $15\beta$, $16\alpha$, and $18$-hydroxylation of testosterone and $17$-oxidation of androstenedione, have been sexually differentiated in mature animals (male/female = 7-200 fold) but not in immature animals. Furthermore, specific cytochrome P450 enzymes were shown to metabolize testosterone selectively at these various positions (Sonderfan et al., 1987)…

In humans, the oxidative metabolism of testosterone occurs predominantly in the liver at the $6\beta$-position, and to a lesser extent at the $15\alpha$, $15\beta$, and $2\beta$-positions. Cytochrome P4503A4 has been shown to be the major testosterone $6\beta$-hydroxylase in human liver, catalyzing testosterone hydroxylation at the $15\alpha$, $15\beta$, and $2\beta$-positions, as well (25). Human liver cytochromes P4502C9 and P4502C19 also have been shown to possess significant testosterone hydroxylase activity (Yamazaki and Shimada, 1997)…

Table A3 (Annex) shows that consumption of beef from hormone treated vs non-treated cattle results in exposure to excess levels of testosterone ranging from 5 to 189 ng/person/day, depending upon the implant used…

The tolerance levels for testosterone levels in uncooked tissues of steers and calves established by the FDA (Ref.: Code of Federal Regulations (CFR) 21, Part 556, Tolerances for residues of new animals drugs in food) are:

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Testosterone (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>0.64</td>
</tr>
<tr>
<td>Liver</td>
<td>1.3</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.9</td>
</tr>
<tr>
<td>Fat</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Based on these levels, consumption of 500 g/day of beef (300 g muscle, 100 g liver, 50 g each of kidney and fat) would result in exposure to approximately 0.6 µg/person/day. The maximum excess exposure to testosterone estimated to occur upon consumption of meat from hormone-treated cattle, 189 ng/person/day (Table A3, Annex) represents 33% of the acceptable level established by the FDA (0.6 µg/person/day) which also represents approximately 1-2% of the daily production rate for testosterone of 32 µg/day estimated for prepubertal girls. However, there is considerable uncertainty associated with the validity of the daily production rate data. It is possible that this value has been over estimated by one to two orders of magnitude, in which case excess testosterone intake from hormone-treated beef could at best exceed the 1% FDA safety margin and at worst be greater than that naturally present…
Testosterone Levels in Human Blood: As expected, men have the highest levels of blood testosterone (Table 1, section 4.1) and the daily production rate has been determined to be approximately 6,500 µg/day (JECFA, 1987). Testosterone levels are much lower and similar in females and prepubertal males. It has been reported that daily production rates of testosterone are between 140 to 240 µg/day in adult women and 32 and 65 µg/day in prepubescent girls and boys, respectively (JECFA, 1987). These data suggest that all females and prepubertal males represent the individuals are greatest risk for adverse health effects that might be associated with exposure to exogenous sources of testosterone…

The toxicological issues of concern include endocrine, developmental, immunological, neurobiological, immunotoxic, genotoxic and carcinogenic effects. Specific hazardous effects are detailed below…

The mutagenicity/genotoxicity of testosterone has been investigated in several studies which are summarised below:

Table. 6: Summary on the studies on mutagenicity and genotoxicity of testosterone

<table>
<thead>
<tr>
<th>Assay</th>
<th>Results</th>
<th>ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mutation ± S-9</td>
<td>Negative</td>
<td>(Richold, 1988)</td>
</tr>
<tr>
<td>Mouse L5178Y TK+/- cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In vivo chromosomal aberrations</td>
<td>Negative</td>
<td>(Richold, 1988)</td>
</tr>
<tr>
<td>Rat bone marrow</td>
<td>Negative</td>
<td>(Richold, 1988)</td>
</tr>
<tr>
<td>Rat spermatogonial cells</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Thus, no genotoxicity has been demonstrated with the limited testing to date.

A low level of covalent binding of testosterone to rat liver DNA has been reported (Barraud et al., 1984).

No information is available on DNA damage induced by testosterone or its metabolites. Testosterone is, however, aromatized to oestradiol, which is metabolized to reactive forms that damage DNA and induce mutations (see section 4.1 above).
Feeding of testosterone has been reported to induce uterine tumours in mice and prostate tumors in rats (Van Nie et al., 1961; Noble, 1977). Whereas the evidence in favour of carcinogenicity was considered sufficient for testosterone in experimental animals, data in humans are limited.

In conclusion, although endogenous testosterone may play a role in the occurrence of prostate cancer, the evidence is currently weak. However, in consideration of the limited data on genotoxicity and taking into account that testosterone might be aromatized to oestradiol, which had found to be genotoxic, no conclusive quantitative estimate of the risk arising from the excess intake with meat and meat products from treated animals can be made. Based on the above mentioned epidemiological data androgenic anabolic steroids including testosterone were considered as probable carcinogenic to humans (IARC group 2 A)

Testosterone is the major androgen secreted by testes in men of adult age. Plasma levels of testosterone are low in women and very low to undetectable in children.

In adolescent boys, puberty is associated with an increasing plasma level of testosterone which exerts direct virilizing and anabolic effects, leading to increases in bone mass and muscle bulk. In adolescent girls with aromatase deficiency, enhanced testosterone levels are associated with pseudohermaphroditism, virilization and polycystic ovaries (Morishima et al., 1995; Mullis et al., 1997).

Continuous administration of exogenous testosterone can induce deleterious effects in the reproduction of male and female mammals. Particularly in the adult male, a sustained increase in plasma level of testosterone administered by ingestion, injections or implants, induces a decrease in secretion of gonadotropins, leading to alterations or arrest of spermatogenesis and azoospernia.

Hormonal imprinting effects of testosterone have been reported in rodents. In the female rat, postnatal androgenization with a single injection of testosterone alters permanently by imprinting the response of uterine cells to oestrogen action (Mena et al., 1992). Moreover, imprinting of female offspring with testosterone results in insulin resistance and changes in body fat distribution at adult age in rats (Nilsson et al., 1998). These changes are similar to those observed in adult female rats or women receiving testosterone. No dose response estimate can be given for this effect yet…

Effects of testosterone on the immune system

There are limited experimental data on the effects of testosterone on immuno response but none on the dose response aspects…
Testosterone (0.9 mg twice weekly for 3 weeks) has been claimed to increase the susceptibility of mice to Plasmodium Chabaudi malaria by imposing restrictions on the genes controlling resistance. This enhanced susceptibility continued for at least 12 weeks after testosterone withdrawal. In contrast the reduction in spleen cell number had completely reversed by this time. The mechanism is considered to involve hormone imprinting (Benter et al., 1997)…

It has been shown that female mice, subsequently treated with testosterone, have reduced burdens of worms compared with non testosterone treated controls. No such effect was observed if testosterone was given after an infective dose of worms was administered (Nakazawa et al., 1997)

In broiler chicks, given 0.1 mg per kg body weight of testosterone, a significant decrease of total leucocytes, lymphocytes and weight of the bursa of Fabricious was noted indicating an immuno suppressant effect of testosterone (Al Afaleg and Homeida, 1998).

In conclusion, these studies are inadequate to enable a judgement to be made on whether meat containing testosterone residues could have an adverse effect on the immune system of consumers.”

161. In addition, the SCVHP noted that currently testosterone, when used for growth promotion purposes is only used in combination with oestradiol 17β, the genotoxic potential of which has been established.

162. The United States, other than referring to the 1999 JECFA assessment, does not put forward any specific argument with regard to this hormonal substance. As regards the 1999 JECFA assessment the SCVHP took issue with the fact that:

110 See 2002 Opinion, Exhibit US - 1, 14f.
At its February 1999 Meeting, the JECFA established for testosterone an ADI of 0.2 µg/kg bw (14 µg/70 kg person) on the basis of a study in eunuchs. This value includes a safety factor of 1000 to protect more sensitive populations and because of the small number of subjects in the study used to determine the NOEL. In that study, oral administration of a dose of 100 mg/day (equivalent to 1.7 mg/kg bw/day) of fine-particle testosterone to five eunuchs had no effect on sexual function indexes while a dose of 400 mg/day restored full sexual function. The dose of 100 mg/day was taken as the NOEL in this study. In another study in postmenopausal women, treatment with 10mg/day methyltestosterone was found to induce signs of virilisation. The ADI for testosterone established by the JECFA (14 µg/person) is greater than the highest excess exposure to testosterone (189 ng/person) that could occur from ingesting hormone-treated beef. However, there are concerns regarding the strength of the study that provided the data for determination of the ADI. First, neither the actual data nor reference to a peer-reviewed publication was provided. Second, the dose-response was limited to two doses and the ADI was estimated from just a single dose where no effect was observed, rather than a curve derived from all the data available.

163. As pointed out above with regard to progesterone, the United States’ reference to the epidemiological studies on the effects of the hormones on post-menopausal women, in the context of an assessment of Testosterone, is equally erroneous.

164. The United States notes, in footnote 57 of its First Written Submission, that bulls account for 29.5% of total cattle slaughtered in the EU 15 (US Exhibit 8), compared with 2% in US. This indicates, according to the US, that the meat consumed in the EU may have endogenous testosterone levels much greater than that produced from steers, which account for a higher proportion of slaughtered animals in US. It is a matter of choice and preference that United States chooses to castrate a high percentage of its male animals destined for beef production. Castration has benefits for ease of management but there are welfare concerns associated with the procedure, and the animals do not grow as rapidly as entire cattle. Indeed, this is one reason why the United States finds it necessary to use hormone growth promoters, i.e. to replace the natural hormones produced in the intact animal and thereby increase weight gain. In the EU, ways of handling young bulls have been developed which fit the type of cattle and husbandry systems found in the EU. The vast majority of the entire male animals slaughtered in the EU are classified as “young bulls” which are less than 24 months old, and may be
as young as 12 months at which stage they are barely sexually mature. The US has not provided any data to support its hypothesis that the meat from such young animals would indeed be much greater than that from steers. Much depends on the age at slaughter, the breed used, and the type of husbandry employed in rearing these animals. The US argument is therefore at best irrelevant in deciding the central issues of the present dispute.

(c) Trenbolone

165. As regards trenbolone, the SCVHP found *inter alia* the following insufficiencies:

The metabolism of TBA appears complex and species dependent. Further investigations of both the metabolic fate and the chemical nature of the covalently bound residues is warranted (Metzler, 1999)…

The metabolism of trenbolone in humans has not been extensively studied. In one study, Spranger and Metzler (Spranger and Metzler, 1991) examined the disposition of 17-β-trenbolone in a single human subject administered 0.04 mg/kg body weight. Urine was collected in fractions for 72 hours after ingestion. The fraction of the first 3-h urine contained the highest concentration of radioactivity and was used for the analysis of metabolites. Of the urinary material, 54 % was present as glucuronides, which contained mostly 17α-trenbolone, 17β-trenbolone and trendione. At least five other polar metabolites, presumably hydroxylated products, were detected in smaller amounts. A total of 54% of the administered radioactivity was found in the urine after 26 hours, and 63% after 72 hours (Spranger and Metzler, 1991). Further analyses of the formation of polar metabolites of trenbolone is essential to the assessment of the risk of repeated dietary exposure of humans to this compound…

Since TBA does not occur naturally, by definition endogenous levels in humans should be zero. Thus, any residues detected in the meat of treated cattle represent excess exposure to individuals consuming the meat…

The FDA (*CFR 21, Part 556, Tolerances for residues of new animals drugs in food*) has set tolerance limits for TBA levels in uncooked tissues of cattle.

<table>
<thead>
<tr>
<th>Tissues</th>
<th>TBA (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>50</td>
</tr>
<tr>
<td>Liver</td>
<td>100</td>
</tr>
<tr>
<td>Kidney</td>
<td>150</td>
</tr>
<tr>
<td>Fat</td>
<td>200</td>
</tr>
</tbody>
</table>
Based on these levels, consumption of 500g of meat/person/day (comprised of 300g muscle, 100g liver, 50g kidney and 50g fat) the acceptable daily consumption of TBA could reach 43 µg/person/day, an amount considerably greater than recommended by the JECFA. This value greatly exceeds the recommended ADI.

The toxicological issues of concern include endocrine, developmental, immunological, neurobiological, immunotoxic, genotoxic and carcinogenic effects. Specific hazardous effects are detailed below.

Feeding of high doses of Trenbolone acetate (TBA) to mice induced a significant amount of liver hyperplasia and tumors; in rats a slight increase in islet-cell tumors of the pancreas was observed (WHO Technical Report No. 696, 1983). A 2-year carcinogenesis bioassay in male and female rats and mice did not provide definitive results on the carcinogenicity of β-TBOH (mentioned in Schiffman et al., 1988)…

In humans, no data are currently available to assess the carcinogenicity of trenbolone.

In conclusion, in consideration of the lack of in vitro short-term assays on mutagenicity and genotoxicity of other TBOH metabolites other than α-TBOH, and in consideration of the equivocal results of cell transformation assays and the in vivo studies, the available information is insufficient to complete a quantitative risk assessment. It has also to be noted that a considerable fraction of TBOH residues seems to be covalently bound to tissues…

Deleterious effects of trenbolone acetate exposure were reported in the reproduction of both male and female mammals of various species (JECFA, 1988). In the adult male, trenbolone acetate administered by ingestion, injections or implants induces a decrease in testis, seminal vesicle and prostate weights and alterations in spermatogenesis. In the adult female, such treatments induce virilization and alteration or suppression of ovarian cycles. In a study involving women volunteers given i.m. doses of 10 mg trenbolone acetate every-other-day during 14 days, disturbances of the menstruation cycle have been reported…
Some data in rodents indicate that administration of trenbolone acetate during the intrauterine or/and perinatal period alters the reproductive function in adults. In a multi-generation study, it has been shown that trenbolone acetate, administered to female rats at dietary concentrations of 3 and 18 ppm between 2 weeks before mating and 3 weeks after birth of youngs exerts effects on reproductive performance which are more marked in F2 pups than in F1 pups of a comparable age. Indeed, female F1 pups from F1-treated parents show signs of virilization, a delay in the mean vaginal opening and the presence of occlusive strands in the vagina or incomplete vaginal opening. Male pups show a delay in the occurrence of testicular descent and a decrease in weights of seminal vesicles, prostate, testes and epididymis. In addition in F2 from both sexes, the adrenal weight is also decreased (JECFA, 1988). These data do not allow a realistic assessment of a dose response relationship…

Investigations on the effects of trenbolone on the immune system are very limited.

A slight, but non statistically significant, immuno depression was seen in male calves given SC implants of trenbolone acetate (140 mg). A statistically significant change was observed when a combination of trenbolone acetate and oestradiol (20 mg) was used. No such change was seen with oestradiol alone. In female calves no such effects were observed (Gropp et al., 1975)...

In conclusion, this information is insufficient to assess the possible impacts of low levels of trenbolone in meat and meat products on consumers.”

166. In its 2002 Opinion the SCVHP found these conclusions to be compounded by data obtained in certain of the 17 studies (studies, n° 2,4 and 10) and more recent research, none of which was considered by the 1988 JECFA report.

167. The United States does not put forward any specific argument as to why the evidence assessed by the SCVHP would not be insufficient. As a matter of fact, the only assessment on trenbolone publicly available is that of JECFA 1988. The SCVHP took into account this assessment but disagreed with a number of its basic findings on the bases of more recent scientific evidence, some of which was generated by the 17 EC studies.

(d) Zeranol

168. As regards zeranol, the SCVHP found that:

“...In humans, the half-life of zeranol plus its metabolites in the blood was 22 h (Migdalof, et al, 1983). Urinary excretion was predominant and included glucuronide and sulfate conjugates. A substantial portion of the dose was not accounted for (23%) and is assumed to be unknown metabolites, possibly including hydroxylated zeranol or ring-opened zearalenone (Metzler, 1999). The half-life of zeranol suggests that this compound plus its derivatives can accumulate in humans consuming zeranol-containing food on a regular basis...

The FDA (Ref.: CFR 21, Part 556, Tolerances for residues of new animal drugs in food) has set tolerance limits for zeranol levels in uncooked tissues of cattle.

<table>
<thead>
<tr>
<th>Tissues</th>
<th>Zeranol (µg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle</td>
<td>150</td>
</tr>
<tr>
<td>Liver</td>
<td>300</td>
</tr>
<tr>
<td>Kidney</td>
<td>450</td>
</tr>
<tr>
<td>Fat</td>
<td>600</td>
</tr>
</tbody>
</table>

For consumption of 500g of meat/person/day (comprised of 300g muscle, 100g liver, 50g kidney and 50g fat) the acceptable daily consumption of zeranol could reach 128 ug/person/day. This value exceeds the ADI by almost 4 fold...

The toxicological issues of concern include endocrine, developmental, immunological, neurobiological, immunotoxic, genotoxic and carcinogenic effects. Specific hazardous effects are detailed below...

The mutagenicity/genotoxicity was investigated in only a few tests, as presented in the following table.

Table 11: Summary of the data on mutagenicity and genotoxicity of zeranol

<table>
<thead>
<tr>
<th>Assay</th>
<th>Result</th>
<th>[ref]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sister chromatid exchange + s-9</td>
<td>Negative</td>
<td>(Scheutwinkel et al., 1986)</td>
</tr>
<tr>
<td>V79 cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOS chromotest + s-9</td>
<td>Negative</td>
<td>(Scheutwinkel et al., 1986)</td>
</tr>
<tr>
<td>REC assay in Bacillus subtilis</td>
<td>Positive</td>
<td>(Scheutwinkel et al., 1986)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Ueno and Kubota, 1976)</td>
</tr>
</tbody>
</table>
These few assays with equivocal results are insufficient for an evaluation of the mutagenic/genotoxic properties of zeranol…

Tritium-labeled zeranol was found to bind to rat liver DNA after treatment with a single dose of 60 µg/kg (Barraud et al., 1984).

DNA adducts of zearalenone (of which zeranol is a metabolite) have been observed in the kidney and liver of female mice treated with a single dose of zearalenone (2 mg/kg, i.p or orally) (Pfohl-Leskovicz et al., 1995). After repeated doses of zearalenone, DNA adducts were recovered in mouse ovaries.

Complete inhibition of DNA synthesis was produced in human peripheral blood lymphocyte cultures at a concentration of 30 µg/mL (Cooray, 1984).…

A two-year oral carcinogenicity study with Fisher 344/N rats given zeranol in the diet at 25 or 50 ppm (1 or 2 mg/kg) showed no treatment-related neoplastic effects (National Tox. Prog. Report no. 235, 1982). With B6C3F1 mice fed zeranol in the diet at doses up to 100 ppm (about 17 mg/kg), no effects were observed with males, but oestrogen-related effects were seen in females in several tissues, as well as myelofibrosis in the bone marrow…

Dose-dependent induction of adenomas and carcinomas of the liver were found in zeranol-treated male and female Armenian hamsters, reaching 100% for adenomas and 75% for carcinomas at the highest dose (Coe et al., 1992). In comparison with DES, zeranol was much more carcinogenic for the liver than expected based on its relative oestrogenic activity.

Zeranol also induced a low incidence of renal tumors of Syrian hamsters (Li and Li, 1987).

No data are currently available on cancer risk for humans linked to meat with zeranol residues.

In conclusion, in consideration of the limited data on mutagenicity/genotoxicity and the clear evidence for an induction of liver adenomas and carcinomas in one animal species (Armenian hamsters) no assessment of the possible carcinogenicity of zeranol can be made…

…Deleterious effects of zeranol exposure have been reported in reproduction of both male and female mammals of various species (JECFA, 1988). In the adult male, a sustained increase in the plasma level of zeranol administered by ingestion, injections or implants induces a decrease in testis, seminal vesicle and prostate weights and alterations or arrest of spermatogenesis. In the adult female, such treatments induce alteration or suppression of ovarian cycles and endometrial hyperplasia. In rodents, a decrease in ovulation rate and litter size has been reported.
In a three generation study of rats receiving zeranol at levels up to 0.20 ppm throughout gestation, it has been concluded that fertility of the offspring is not affected (JECFA, 1988). However, male mice exposed in utero to zeranol (150 µg/kg of body weight injected on days 9 and 10 of gestation) show testicular abnormalities (regressive changes in the germinal epithelium and Sertoli cells, and immature morphology of Leydig cells) when testes are examined at 45 days of postnatal life (Perez-Martinez et al., 1997). No estimate of the dose-response relationship for these effects can be made…

No relevant data on the effects of zeranol on the immune system were found.

In conclusion, the available data do not allow a quantitative estimate of the risk arising from exposure to zeranol residues. In addition, further data are needed on the nature of the metabolites formed in bovines.”

169. As for Trenbolone, the SCVHP, in its 2002 Opinion, found this analysis to be compounded by data obtained in certain of the 17 studies (studies, n° 2, 4 and 10) and more recent research.

170. The United States does not put forward any specific argument as to why the evidence assessed by the SCVHP would not be insufficient. As a matter of fact, the only assessment on zeranol publicly available is that of JECFA which dates back to 1988. The SCVHP took into account this assessment but disagreed with a number of its basic findings on the bases of more recent scientific evidence, some of which was generated by the 17 EC studies. Moreover, the most recent study on zeranol and the risks associated with its administration to meat producing animals is done by independent US scientists mentioned above and it clearly invalidates the findings of the 1988 JECFA opinion.

(e) MGA

171. As regards MGA, it should be recalled the finding of the Appellate Body (at para. 201) that no risk assessment had been performed. There is currently no international standard or recommendation on MGA, as Codex has not adopted one. JECFA assessed MGA for the first time in 2000 (and in 2004 as regards the

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calculation of the MRL only), but this has not yet led to the adoption of a standard. If one examines the evidence that served as the basis of the 2000 JECFA report it can be seen that nearly all the studies referred to therein date from the 1960s and 1970s. These very old studies constitute in fact the evidence which the defending parties have refused to provide to the European Communities, despite its repeated requests on the grounds that they are confidential.\footnote{On this also Appellate Body Report, \textit{EC- Hormones}, at para. 201.} In the absence of a Codex standard, the opinion of JECFA becomes irrelevant, for the additional reason that it failed to take into account the more recent data generated by the 17 EC studies and the 2002 SCVPH assessment.

172. The SCVHP found that:

Melengestrol acetate (17-acetoxy-6-methyl-16-methylenepregna-4,6-diene-3,20-dione, MGA), a progestogen, is a synthetic anabolic steroid used for improved efficiency in feed utilization, growth stimulation and estrus suppression of feedlot heifers (Federal Register, 1968 and 1969). It is also effective as an estrus synchronization agent for cattle (Zimbelman, et al., 1970). In intact heifers, treatment with MGA causes significant increases in pituitary luteinizing hormone (Fed. Regist., 1968). It appears that MGA blocks the cyclic surge in luteinizing hormone that produces ovulation, but allows the tonic release of luteinizing hormone that synergizes with follicle stimulating hormone for oestrogen production. The progestogen activity of MGA is approximately 30 times greater than that of progesterone, as measured in the rat (Duncan, et al., 1964). MGA had no androgenic activity and very little oestrogenic activity (Duncan, et al., 1964).

In humans, the onset of menses is delayed by a dose of 7.5 or 10 mg MGA/day in normal ovulating women, but not by a dose of 5 mg MGA/day (Duncan, et al., 1964). Based on these and other data from human studies, a minimal effective daily dose of 0.7 mg MGA and a no-effect daily dose of 0.4 mg MGA was derived for MGA in women (Lauderdale, et al., 1977). Using the maximum residue levels of MGA in beef muscle and fat (less than 10 ppb after 48h withdrawal), it was further calculated that daily consumption of 100 pounds of MGA-fed heifer meat would not exceed the no-effect dose.

Pharmacokinetics and biotransformation of melengestrol in animals
MGA metabolites formed in cattle have been detected, but not identified (Krzeminski, et al., 1981). Cattle fed radiolabeled MGA excreted MGA and its metabolites mostly in feces (87%), with 13% in urine. Approximately 15% of the MGA was excreted intact (Lauderdale, et al., 1977). In fat, 86% of the MGA was intact, but only 48% was not metabolized in muscle and 29% in liver and kidney (Krzeminski, et al., 1981).

In vitro metabolism of MGA by Arochlor-induced rat liver microsomes yielded seven monohydroxylated and five dihydroxylated metabolites separated by HPLC and identified by HPLC/MS (Metzler, 1999). The major metabolites produced by the rat liver microsomes were also observed with bovine liver microsomes.

**Melengestrol disposition in the target animal**

The highest concentration of MGA and its derivatives was found in the liver, although fat was found to be the actual target tissue for MGA. In studies of pregnant heifers fed MGA at 0.4 mg/head daily, MGA concentrations of 10-20 ppb were found in the fat, but the levels decreased to less than 10 ppb at 48 h after withdrawal (Lauderdale, et al., 1977).

**Pharmacokinetics and biotransformation of melengestrol in humans**

The half-life of orally administered MGA to women was estimated to be 3.5 days for doses of 3 to 5 mg (Cooper, et al., 1967). MGA is extensively metabolized in women to more than 20 compounds, with 74% excreted in urine and feces. Intact MGA, as well as its glucuronide and sulfate conjugates, were identified in urine. Two of the metabolites have been tentatively identified as the 2α-hydroxy and 6-hydroxymethyl derivatives (Cooper, et al., 1967).

**Assessment of exposure to melengestrol from consumption of hormone-treated beef**

Only limited data are available concerning MGA residues in treated cattle. It is an orally active progestogen that is mixed in animal feed to provide a daily consumption level of 0.2 to 0.8 mg. MGA is reported to be located mainly in fat at concentrations ≤ 25 µg/kg. The FDA (CFR 21, Part 556, Tolerances for residues of new animal drugs in food) has set the tolerance level for MGA at 25 µg/kg in the fat tissue of treated cattle.

The toxicological issues of concern include endocrine, developmental, immunological, neurobiological, immunotoxic, genotoxic and carcinogenic effects. Specific hazardous effects are considered below.

**Mutagenicity and genotoxicity of melengestrol**

No information is available.
DNA adducts and DNA damage

No information is available.

Carcinogenicity

In female SHN mice, MGA (10 mg pellets implanted subcutaneously every two months) slightly increased the incidence of mammary tumors, but not the incidence of preneoplastic hyperplastic alveolar nodules (Nagasawa, et al., 1988).

In conclusion, in view of the lack of data on mutagenicity / carcinogenicity and on DNA interactions and in consideration of carcinogenicity studies conducted only in one animal species, these data are inadequate to assess the carcinogenetic potential of MGA.

Effect of melengestrol on growth and reproduction

Melengestrol acetate can block ovulation and the menstrual or estrous cycle in females from various species. In addition, it is capable of increasing the serum prolactin concentration of mice fed MGA at a daily rate of 0.2-0.8 mg (Lauderdale et al., 1977). Heifers implanted with MGA for improving growth performance show two- to three-fold increase in serum oestradiol concentrations (Henricks et al., 1997). This effect is likely due to the presence of large persistent follicles on ovaries occurring in response to the increase in LH pulsatility induced by MGA treatment (Anderson and Day, 1994; Imwalle et al., 1998). These data do not allow an estimate of the dose response relationship.

Effect of melengestrol on the immune system

Available data are very limited. The only study uncovered is an investigation of the effects of MGA on the ability of cows to remove E. coli that have been introduced into the uterus. The results of this study were inconclusive (Zimbelman RG. et al., 1970)

The information is insufficient to make a scientific judgement on whether MGA may cause effects on the immune system at levels which could occur in meat treated with MGA growth promoters.
In conclusion, Melengestrol is an orally active progestogen. The toxicological issues of concern include endocrine, developmental, immunological, neurobiological, immunotoxic, genotoxic and carcinogenic effects. As indicated above, the data available on the different issues does not allow a conclusive assessment either of the amounts of residues in edible tissues (in particular no quantitative data are available on the concentration of metabolites in edible tissues) or the nature of toxicological effects. This implies that the available information is insufficient for a quantitative estimate of the risk to the consumer of meat and meat products derived from treated animals."\(^{114}\)

173. In its 2002 Opinion, the SCVHP found these conclusions compounded by data obtained in certain of the 17 studies (studies n° 4, 5 and 10).\(^{115}\)

174. The United States does not put forward any specific argument as to why the evidence assessed by the SCVHP would not be insufficient. It does not even refer, in this context, to the fact that MGA, in the meantime (2000), has been assessed (for the first time) by the JECFA.\(^{116}\) As a matter of fact, that assessment has been taken into account by the SCVHP in its 2002 Opinion. The SCVHP noted that in the JECFA report no original data had been presented and that the majority of references were to reports that had not been published in the peer-reviewed scientific literature.\(^{117}\)

175. Moreover, the United States referred the Panel to a draft 2005 report from the UK CVP, which it considers to be supportive to its arguments. This is far from being entirely correct. The draft 2005 UK report states in particular:

As has been noted in this report, and acknowledged in the SCVPH Opinion, there are important gaps in the evidence base that preclude producing definitive risk assessments for 17β-oestradiol or the other five hormonally-active substances. Not all data gaps are equally important for the purposes of risk assessment and the Working Group highlighted a number that could improve future risk assessments. As an example, it would be helpful if the CVMP and JECFA could make available data on pharmacokinetics and metabolism of assessed compounds that were supplied in manufacturers’ dossiers. This openness and transparency would allow greater public scrutiny of the facts and confidence in the hazard and risk assessments produced.

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\(^{114}\) See 1999 Opinion, Exhibit US - 4, p.66-68.


\(^{116}\) See above.

\(^{117}\) Ibid., p. 16.
7. The Working Group felt that none of the basic issues could be addressed without a structured approach. There was a need to establish precisely the:

relationships between the potential use of growth-promoters (including over-use) and concentrations of residues in meat;

levels of exposure in consumers (i.e. taking account of intake, absorption, bioavailability and metabolism); and

dose-response relationships for the effects of the hormonally-active substances (and their metabolites) in experimental animals or in humans.

further data on lipoidal oestrogens, possible bioaccumulation and possible synergistic effects of cocktails of hormonal substances would also be desirable

8. The Working Group noted specific needs:

To establish in humans the detailed relationship between systemic exposure to specific hormonally-active substances and the amount of meat consumed from treated animals.

To establish in experimental animals the relationship between intake of hormonally-active substances, or their metabolites, and target-organ effects (selecting the likely most sensitive target organ depending on the nature of the activity of the compound). This study to be conducted for adults and then fetal and/or neonatal exposure to be considered.

To consider lipoidal esters of oestrogen in future studies of the possible passage of oestrogen in implants through cattle to humans. The bioavailability and metabolism of lipoidal esters following ingestion should be investigated to allow the biological significance of the oestrogens to be assessed.

To carry out studies to confirm whether the ADI for pre-pubertal boys could be exceeded if they consumed a standard\textsuperscript{118} 500g portion of meat from an animal that had been treated with a number of hormonal implants. If confirmed this would be of concern.

9. The following need to be established in order to improve future risk assessments:

the precise relationship between the potential use of growth-promoters and concentrations of residues in meat

levels of exposure in consumers

\textsuperscript{118} The JECFA veterinary hypothetical diet assumes daily consumption of 300g muscle, 100g liver, 50g kidney and 50g fat.
dose-response relationships for the effect of hormonally active substances (and their metabolites) in experimental animals and humans

the bioavailability, metabolism and possible bioaccumulation of lipoidal esters of oestrogen following ingestion of meat from implanted cattle

the possible synergistic effects of cocktails of hormonal substances

a validated technique to detect and assign low residual concentrations of oestradiol in the finished edible products to natural sources or implant residues.119

176. In conclusion, there is no doubt that the 1999-2002 SCVPH Opinions constitute the only currently available risk assessment on MGA. They are based on the most recent, peer-reviewed, pertinent information that is now available publicly from the European Communities. The SCVPH assessment came to the conclusion that there are a number of risks associated with the administration of MGA to meat producing animals because of their residues and that the current state of scientific knowledge does not permit a more definitive risk assessment to be done.

3. The provisional prohibitions have been adopted on the basis of the available pertinent information

177. The United States claims that the provisional ban has not been adopted “on the basis of available pertinent information.” The United States argues that:

Indeed, as has been discussed above, the studies relied on by the EC as a basis for its provisional ban do not in fact demonstrate a risk associated with residues from meat and meat products from cattle that have been treated with hormones for growth promotion purposes according to good veterinary practice.120 [emphasis added]

178. First, it is not clear where the issue of studies demonstrating or not a risk for the five hormonal studies would have been “discussed above.” As seen in the previous section, the United States does not discuss any of the evidence assessed in the SCVHP’s Opinions or contest any of the conclusions drawn by the SCVHP

119  See Exhibit US-20, at pages 4-5.
120  US First Written Submission, at para. 130.
on the five hormonal substances in question. Instead, it limits itself to wholesale references to JECFA reports, ‘25 years of intensive studying’ and the assessments of “numerous national regulatory bodies”, which are neither publicly available nor produced here for the purposes of these proceedings.

179. Second, the assumption that a risk has to be demonstrated in order to justify a measure adopted on the basis of Article 5.7 of the *SPS Agreement* is simply erroneous. The whole point of evidence being “insufficient” is that it does not allow the clear demonstration of a risk. If a risk can be demonstrated, it means that there is sufficient evidence to carry out a proper risk assessment.

180. Thus the United States has not put forward any argument as to why the provisional ban would not have been adopted on the basis of the available pertinent information.

181. The Panel, on its own motion, in Question 68, has raised the issue of whether the standard of “on the basis of available pertinent information” would be that of a “rational relationship” as it is in Article 5.1. In reply to that question the European Communities has argued that there must necessarily be a difference between the objective or rational relationship between sufficient scientific evidence and a measure within the meaning of Article 5.1, on the one hand, and insufficient evidence and a measure within the meaning of Article 5.7, on the other.\textsuperscript{121} Under Article 5.1 a convincing link is required between the evidence and the measure. Under Article 5.7 a mere doubt must be sufficient. In the previous section, the European Communities has summarised for each of the five hormonal substances the evidence that the SCVHP has assessed and found to be clearly insufficient. While inconclusive in terms of demonstrating a risk, that evidence does nevertheless point to the possible occurrence of certain adverse effects, which invalidate or put into serious doubts previously held assumptions about the safety of these hormones by the defending parties and Codex/JECFA.

\textsuperscript{121} EC Replies to Panel Questions, para. 248.
4. **The European Communities has not violated its obligation to seek to obtain the additional information necessary for a more objective assessment of risk**

182. The United States does not actually argue that there is a violation of the obligation to seek additional information. To the contrary, the United States states that “there is simply no need to obtain the additional information necessary for a more objective assessment of risk.”\(^{122}\)

183. Obviously, the European Communities takes a different view as it is of the opinion that the current evidence is insufficient to conduct a definitive risk assessment. Therefore, the European Communities does see itself under an obligation, under Article 5.7 of the *SPS Agreement*, to seek additional information. Indeed, it has specifically laid down that obligation in Directive 2003/74/EC.\(^{123}\) As a matter of fact, the European Communities has already undertaken initiatives to seek additional information. In particular, it has issued a new call for scientific data and research from 2002 onwards, on substances with hormonal activity which may be used for growth promotion purposes in bovine meat.\(^{124}\)

5. **The European Communities has not violated its obligation to review the provisional measure within a reasonable period of time**

184. The United States argues that the provisional ban has “in effect been in place for over fifteen years” and that this was not a reasonable period of time “especially given the fact that the provisional ban addresses substances as intensively reviewed and studied as the five hormones at issue.”\(^{125}\)

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\(^{122}\) US First Written Submission, para.132.

\(^{123}\) See Article 1(9) of Directive 2003/74/EC.

\(^{124}\) The call has been published in the C Part of the Official Journal of 28.09.2005 (N° 238, p. 6) and is available at the following link: [http://europa.eu.int/eur-lex/lex/LexUriServ/site/en/oj/2005/c_238/c_2382005050928en00050006.pdf](http://europa.eu.int/eur-lex/lex/LexUriServ/site/en/oj/2005/c_238/c_2382005050928en00050006.pdf); see also EC Reply to Panel Questions, at para. 264.

\(^{125}\) US First Written Submission, paras 133 and 134; see also US Replies to Panel Questions, at paras. 78 and 79.
185. This argument is flawed in a number of respects.\footnote{126} It is erroneous to apply a review requirement to a measure before that measure has even come into existence. This is, however, what the United States does in arguing that the provisional ban is nothing but an extension of the original ban dating back to 1989. Such reasoning simply ignores the fact that a responsible government has adopted a measure on the basis of a given motivation and pretends to be able to apply an outside judgment to what the situation “in effect” is. That flawlessness becomes even more apparent if one follows the course of such reasoning: It raises the question how the United States explains what it is the European Communities has actually done between 1998 and 2003 if not to review the measure in question.

186. In the view of the European Communities, and as explained in reply to the Panel’s Question 71, a requirement to review a measure “within a reasonable period of time” can only apply as of the coming into effect of the provisional measure in question. In the light of the time it took to review the original measure (1998-2002) it can hardly be argued that a reasonable period of time has actually already elapsed.

187. The European Communities has moreover pointed out that Directive 2003/74/EC contains an obligation to “keep the measures applied under regular review with a view to timely presentation […] of any necessary proposals.”\footnote{127} Regular review certainly implies reacting, as appropriate, to new evidence or information that may appear. As a matter of fact, the only new information that has come to the knowledge of the European Communities is the recent draft assessment of the UK Group. That draft report has already been forwarded to European Food Safety Authority (EFSA) for review.\footnote{128} Equally, should the recent call for new scientific information (see above under point 3) yield any new evidence, such evidence would also be assessed by EFSA without any undue delay.

188. In conclusion, the United States, which has the burden of proof, failed not put forward any convincing arguments to support its claim that the European

\footnote{126} The European Communities will not go again into the issue of how “intensively” the five hormonal substances have in fact been reviewed. It refers the Panel to the arguments set out in sections above.

\footnote{127} See Article 1(9) of Directive 2003/74/EC.

\footnote{128} EC Replies to Panel Questions, paras. 259-264.
Communities has violated Article 5.7 of the SPS Agreement in adopting a provisional ban on the five hormonal substances progesterone, testosterone, zeranol, trenbolone and MGA.

C. The ban on Oestradiol 17β is in conformity with Article 5.1

189. The United States claims that the (permanent) ban on oestradiol 17β is not in conformity with Article 5.1 of the SPS Agreement. It raises two arguments namely that the EC Opinions (i.e. the opinions of the SCVHP) do not constitute risk assessments within the meaning of Article 5.1 and that the results of these opinions do not rationally relate to or reasonable support its import ban. The European Communities has to a great extent already responded to these arguments in its replies to the Panel’s questions. It will, in the following, summarise and, where appropriate, complement these replies.

1. There is a risk assessment within the meaning of Article 5.1 and Annex A Point 4 of the SPS Agreement

190. The United States contends that the SCVHP opinions relied on by the European Communities do not constitute “risk assessments” within the meaning of Article 5.1 of the SPS Agreement.129

191. As a preliminary remark and as the European Communities has pointed out in its reply to Question 24 of the Panel, there is a difference between a scientific risk assessment in the narrow sense clearly referred to here by the United States and the risk assessment within the meaning of Article 5.1 and Annex A Point 4 of the SPS Agreement.130 The latter, as has been stated by the Appellate Body, also comprises a risk management stage which is the responsibility of the regulator to carry out and not of the scientific bodies.131 The United States concentrates its arguments on the alleged flaws in the scientific risk assessment of the SCVHP and it is to those that the European Communities will reply.

129 US First Written Submission, paras. 137 – 139.
130 EC Replies to Panel Questions, para. 135ff.
131 Risk assessment, thus, within the meaning of Article 5.1 and Annex A Point 4 is a notion closely linked to the concept of “risk analysis” developed by Codex.
A second preliminary remark is that all parties to this dispute agree on the relevance of the risk assessment techniques developed by Codex recently. Indeed, Article 5.1 itself points to the relevance of risk assessment techniques developed by relevant international organisations. Furthermore, the SCVHP has explicitly based its assessment on the three elements of risk identification, risk characterization and exposure assessment recommended and applied by the Codex. A few qualifications, however, apply. First, risk assessment criteria as they have been developed by the dispute settlement bodies are clearly more relevant to the application of the *SPS Agreement* than those developed by international scientific bodies. This follows naturally from the fact that it is the former’s duty and privilege to interpret the provisions of the *SPS Agreement*. Second, it should be noted that there is no Codex standard specifically on the risk assessment of effects of residues of veterinary drugs. There only exists a general standard on microbiological assessment. Third, it should be pointed out that Codex techniques or standards exclusively apply to risk assessments on food safety and not to other risk assessments such as those for animal health and environmental risks. This is of relevance here insofar as the SCVHP Opinions also discuss environmental risks of the hormonal substances in question and some of the 17 EC studies have generated for the first time pioneering results in these areas.

With these preliminary remarks the European Communities will now address the specific arguments raised by the United States as to why the SCVHP assessment does not complete the three step analysis (hazard identification, hazard characterization, exposure assessment) it has itself set as a standard of its analysis.

(a) **Hazard identification**

The United States actually does not take issue with the hazard identification undertaken by the SCVHP, merely pointing out that “there is no great challenge to completing this first step in a hormone risk assessment.”

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132 Codex defines hazard identification as « The identification of biological, chemical and physical agents capable of causing adverse health effects and which may be present in a particular food or group of foods. 

133 US First Written Submission, para. 140.
195. Rather, the United States’ argument is that the SCVHP’s assessment stops/or predominantly focuses on this first step failing to hone the identified general hazards down through hazard characterisation and an exposure assessment in order to demonstrate a specific risk to consumers.134

(b) Hazard characterisation

196. Thus, the United States takes issue with the way the SCVHP has undertaken a hazard characterisation.135 The argument seems to be that no or no adequate dose response assessment would have been carried out.

197. Hazard characterization is defined by Codex as:

The qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents which may be present in food. For chemical agents, a dose-response assessment should be performed. For biological or physical agents, a dose-response assessment should be performed if the data are available.136

198. A dose response assessment, in turn is defined as

The determination of the relationship between the magnitude of exposure (dose) to a chemical, biological or physical agent and the severity and/or frequency of associated health effects (response).

199. The following remarks apply:

200. One, the United States’ equation of hazard characterization and dose-response assessment is clearly erroneous. The above definition plainly refers to the possibility of either a quantitative or a qualitative evaluation. While a dose-response assessment is a quantitative evaluation, a qualitative evaluation may equally be done, in particular in the absence of available data on dose-response. That is confirmed by the last sentence of the definition which recognises that data may not be available on biological or physical agents. More generally, it is

134 US First Written Submission, para. 142.
135 US First Written Submission, para. 143.
confirmed by the Appellate Body which stressed that a risk assessment within the meaning of Article 5.1 does not necessarily require a quantitative evaluation.137

201. Moreover, it should be further clarified that it is generally recognised that for substances which have genotoxic potential (as is the case with oestradiol 17β) a threshold can not be identified. Therefore it cannot be said that there exist a safe level below which intakes from residue should be considered to be safe. Therefore the fact the doses used in growth promotion are low is not of relevance.

202. Thus, the argument of the United States that there is no hazard characterization is incorrect.

(c) Exposure assessment

203. Equally flawed is the United States’ claim that the SCVHP Opinions do not complete an exposure assessment.138

204. The Codex defines exposure assessment as follows:

> The qualitative and/or quantitative evaluation of the likely intake of biological, chemical and physical agents via food as well as exposures from other sources if relevant.139

205. The United States essentially makes three arguments concerning pathway/residue analysis,140 no risks of abuse and low bioavailability.141 But none of these arguments demonstrated that the Opinions of the SCVHP fail to complete an exposure assessment.

206. In conclusion, therefore, the United States has failed to demonstrate that the SCVHP Opinions do not constitute a scientific risk assessment (as part of an overall risk assessment within the meaning of Article 5.1, i.e. a “risk analysis” in Codex parlance). Moreover, what the United States does also not explain is that its own responsible health authorities have, for the first time since 2002, declared

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138 US First Written Submission, paras 144 – 146.
139 See *Codex Alimentarius Commission*, 14th Procedural Manual, at p. 46.
140 US First Written Submission, para.145.
141 US First Written Submission, para.146.
that oestradiol 17β is proven to be a human carcinogen and it is now listed as such, since 2002, in the USA Annual Report on Carcinogenesis. This latest report for instance states inter alia the following:

Steroidal estrogens also occur naturally in plants. Currently, more than 360 plants have been identified that have estrogenic activity. A few plants contain the principal estrogens found in mammals, estradiol and estrone (Setchell 1985). Meat and milk also may contain estrogens (Collins and Musey 1985). Veterinary use of steroidal estrogens (to promote growth and treat illnesses) can increase estrogens in tissues of food producing animals to above their normal levels.142

On the basis of the most recent evidence from all sources, the US authorities concluded that “steroidal estrogens are known to be human carcinogens based on sufficient evidence of carcinogenicity in humans, which indicates a causal relationship between exposure to steroidal estrogens and human cancer.” For this reason, the 2002 listing of steroidal estrogens as known to be human carcinogens now “supersedes the previous listing of specific estrogens in the Report on Carcinogens (RoC) and applies to all chemicals of this steroid class.”

2. The ban on Oestradiol 17β is based on the risk assessment

The second argument the United States put forward in order to demonstrate that the ban on Oestradiol 17β is not in conformity with Article 5.1 of the SPS Agreement is that that measure would not be “based on” a risk assessment.143 The United States rightly points out that “based on” according to the Appellate Body signifies that “the risk assessment must sufficiently warrant – that is to say – reasonably support – the SPS measure at stake.”144 However, its arguments as to why the SCVPH’s opinions would not reasonably support the ban on oestradiol 17β are flawed.

The United States claims that the SCVHP only identifies “theoretical risks from oestradiol 17β generally, but fail to address the relevant risk – that from arising

143 US First Written Submission, paras 148 – 163.
from the presence in meat of residues resulting from the administration to animals, according to good veterinary practice, of any of the six hormones for growth promotion purposes.¹⁴⁵ It discusses specifically two issues, namely: genotoxicity and carcinogenicity (at paras. 153-156) and endocrine development (at paras. 157-160).

210. In conclusion, the United States fails to demonstrate that the scientific risk assessment carried out by the SCVHP does not reasonably support the measures adopted.

211. Not only does the SCVHP’s assessment support the ban on oestradiol 17β, but more recent research – as already explained above - equally confirms and further reinforces that that measure is warranted.

D. There is no violation of Article 3.3 of the SPS Agreement

212. Finally, the United States alleges that the European Communities has violated Art.3.3 of the SPS Agreement. The United States bases itself on the above argument that the ban would not be in conformity with Article 5.1 of the SPS Agreement.¹⁴⁶

213. The European Communities does not contest that the ban on oestradiol 17β is not based on international standards. The only relevant standard is the Codex recommendation on MRLs for oestradiol 17β. The European Communities, however, has decided not to set MRLs as recommended by Codex, but instead to prohibit the use of oestradiol 17β for growth promotion purposes altogether.

214. That decision is based on a comprehensive risk assessment which, as has been demonstrated above is not in violation of Article 5.1 of the SPS Agreement.

215. The United States’ claim on a violation of Article 3.3 of the SPS Agreement, therefore, must fail.

¹⁴⁵ US First Written Submission, para. 160.
¹⁴⁶ US First Written Submission, para.164.
CONCLUSION

216. In this submission the European Communities has demonstrated that the United States has failed to rebut the EC claims in respect of the systemic violations of the DSU. The European Communities considers that under the DSU it is not allowed for a retaliating Member to adopt a lean-back-and-wait-attitude in the presence of a compliance measure that another WTO Member has adopted in good faith. Furthermore, if the Panel were to decide to take a position on the substantive issues – even though this is not necessary for a satisfactory solution of this dispute - the European Communities has demonstrated that there exists a real risk for human health related to the use of hormones used in meat for growth promotion purposes which justifies its measure.

217. For all the reasons set out thus far, the European Communities would respectfully ask the Panel to find that the United States is in violation of its obligations under Articles 23.1, 23.2(a), 21.5, 22.8 and 3.7 of the DSU and Articles I and II GATT.
# LIST OF EXHIBITS

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