COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COC)

Guidance Statements:

G07- Alternatives to the 2-year Bioassay – Introduction, parts a and b - first draft

Eastmond, D.A., Vulimiri, S.V., French, J.E., Sopnawane, B. (2013) The use of genetically modified mice in cancer risk assessment: challenges and limitations. Crit.Rev. Tox. 43(8)611-631

Nambiar PR, Morton D.(2013) The rasH2 mouse model for assessing carcinogenic potential of pharmaceuticals. Toxicol Pathol.;41(8):1058-67.

These references are attached. They are not being made publicly available for copyright reasons

Secretariat
October 2014

COMMITTEE ON CARCINOGENICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT (COC)

Guidance Statements:

G07- Alternatives to the 2-year Bioassay – Introduction, parts a and b - first draft

Email from a COC Member in response to previous request for comments

Secretariat
October 2014

Subject: Guidance Statement G07

From: COC Member
Sent: 22 October 2014 17:30
To: COC Secretariat
Subject: RE: COC - G07 for review

Hi
I think the assessment of the current alternatives could be useful but I think the review needs to be much shorter and focused than the current document. I would recommend a review format which might be something like:

Rationale: What was the assay developed to achieve? What advantage over the conventional study was it aiming for?
Brief description: No more than a paragraph
Performance: How has the assay been assessed and does it achieve what it set out to do?
Acceptance and usage: Has the assay been accepted by any regulatory authorities? How widely is it used and for what purpose?
Overall comments: A short conclusion.

I expect you could produce something like this from your current document quite easily. If not I would question the value given all the other demands there are on you.

Given the choice between putting effort into this and into a review of emerging strategies, I think a review of emerging strategies during 2015 would be more useful given all the effort in recent years which should start to produce evaluations in the next year or two.

I hope this is helpful.

Best wishes

From: COC Secretariat
Sent: 22 October 2014 10:24
To: COC Member
Subject: RE: COC - G07 for review

Hi,

Apologies for not replying to your email previously, I have been busy with work for COM.

In response to your comments, we do intend to address the Emerging Strategies as part of this series of Guidance documents which will be based on the initial discussion paper we presented earlier. We envisaged this guidance document to simply comment on the applicability of the currently available alternative assays – even if it means we say we don't think they're of value. Do you think this will be useful?

Thank you for your input

Best wishes

From: COC Member
Sent: 19 September 2014 12:26

To: COC Members
Cc: COC Secretariat
Subject: RE: COC - G07 for review

Hi Karin

Sorry to be late in replying but I have been struggling with this paper.

The major issue I have with the paper is that I am not sure what it is trying to do. I think this reflects the confusion in the field of alternatives to the 2 year bioassay which is that it is also not clear what they are trying to do. I think there are to main reasons to look for alternatives, the first is to reduce the cost, time and number of animals used in assessing carcinogenic potential – getting to the same place as we are now but using less resource. The second is to improve the accuracy of the prediction of carcinogenic potential for humans in terms of whether a chemical can cause cancer and if so what is the dose response – getting to a different, more relevant, place than we are now.

The other issue which causes problems is the idea that there will be a study for study substitution in bringing in alternatives. I think this is increasingly unlikely and we need to compare different carcinogenicity assessment strategies. The current strategy could be described as:

1. Assess genotoxicity by chemical structure and in vitro experimentation.
2. Assess other potential mechanisms of carcinogenicity by general and targeted toxicology studies.
3. If it looks unlikely to be carcinogenic or it looks potentially carcinogenic but you want to be sure or to quantify the degree of carcinogenicity, then do 2 year assays.
4. Once you have done the assay do more investigative work if the result looks anomalous.

There is an increasing body of opinion that says do we really need to go to the expense, delay and use the large number of animals in step 3. This is the line being taken in the ICH programme which is running step 2 and 3 for the next few years and is then going to check out the results with the plan to drop stage 3 in many cases. There has also been a lot of work in Europe on alternative carcinogenicity assessment strategies funded by the EU.

My conclusion is that it would be more valuable to prepare a commentary on Emerging Strategies in Carcinogenicity Assessment rather alternatives to the 2 year bioassay against the criteria of either improving accuracy/relevance or reducing animals, time, cost. If we do want to review the studies you have selected then I think a systematic analysis of how they perform against the criteria of resources and of relevance/accuracy would be easy to do. It would also be useful to provide a view of how these studies would fit into an overall carcinogenic potential assessment strategy.

I hope that this is seen as a positive suggestion as a way to build on the excellent work you have done so far.

Best wishes

From: COC Secretariat
Sent: 15 September 2014 10:19
To: COC Members
Cc: COC Secretariat
Subject: RE: COC - G07 for review

Thank you to those I have received comments from. Please can I gently remind those of you who did want to input, please can I have comments by Monday next week (23rd Sept.).

Thanks

From: COC Secretariat
Sent: 18 July 2014 13:07
To: COC Members
Cc: COC Secretariat
Subject: COC - G07 for review

Dear COC Members,

Following on from yesterday's meeting when there was insufficient time to consider this item, please find attached a word version of the Guidance statement G07 - Alternatives to the 2-year bioassay. If you have comments on this first draft, please either add changes in the word version or simply jot your thoughts down in an email. Furthermore, if there are significant omissions you'd like to see included please let me know. I can then refine the content prior to the next meeting.

Please provide comments by **September 12th 2014.**

Thanks in advance for your help!

Best wishes