



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4797

Title: Is the validation of biocides against the hepatitis B virus by the use of surrogates possible?

Reviewer code: 00502973

Science editor: Cui, Xue-Mei

Date sent for review: 2013-07-24 14:01

Date reviewed: 2013-07-28 17:49

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input checked="" type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The manuscript titled "Is the validation of biocides against the hepatitis B virus by the use of surrogates possible?" by Andreas Sauerbrei reviewed the methods currently available in the verification of virucidal efficacy of disinfectants against HBV and introduced the method with primary duck embryonic hepatocytes. This is an interesting topic. However, concerns exist preventing its acceptance. 1. The author used 4 pages to present the protocol of in vitro duck hepatitis B virus model for testing virucidal efficacy of biocides in a 14-page paper. I suppose this is a review paper. The author should make comments on experimental method or result rather than present the protocol in a review article. Such protocol should be presented in detail in a research report. Alternatively, the author should submit such a paper to other journal focused on methodology. 2. The English language in this paper needs to be polished. Some sentences are too long and too complex to be understood. For example, "A German guideline for testing the virucidal activity of chemical disinfectants in the human medical area characterize disinfectants effective against enveloped viruses as biocides with limited virucidal activity in contrast to disinfectants with virucidal activity effective against non-enveloped plus enveloped viruses[19,20]." at page 4, "Recently, more practice-relevant methods have been developed testing the viral infectivity after exposure to viruses dried on non-porous surfaces simulating application conditions found in actual practice[23]." at page 6, and "It has been concluded that the differences that exist between DHBV and HBV principally concern the difference between the hosts they infect and the nature of the disease they produce, and have no bearing on the ability of disinfectants to abolish infectivity of the viruses[38]." at page 8. Specific: 1. Page 6: "For in vitro infectivity testing, the use of the hepatoma cell line HepG2 described in the literature[22,27] has to be regarded as very doubtful." The author should clarify if



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

there is any reference against this method. Similarly, also in this page, "In comparison, re-differentiated HepaRG cells[28] are well accepted and reproducible as HBV infectivity system ." The author should clarify if there is any reference supporting this method. 2. I have a question about the last sentences on page 6. As both the HepaRG cell and the Tupaia hepatocyte HBV infection models require high viral concentration, I suspect their qualification as methods to test the virucidal activity of biocides. If the biocides cannot kill all the viruses, the survived virus still possesses the capacity of infection. However, partial killing will reduce the viral concentration and would result in a negative result when it is tested by these models which requires high viral concentration for successful infection. 3. Page 8: "It is of great value that the DHBV is maintained in domestic duck flocks through vertical transmission from viremic ducks, the virus infects the developing liver in ovo and is not recognized sufficiently by the host immune response to produce hepatitis and liver disease or eliminate the virus[34]." As I know, the host immune system recognizes the invading pathogen to elicit immune response. The pathogen is not recognized by the immune response. 4. References: 5. The source of some references like No. 17 and No. 41 should be showed, e.g. the journal in which it was published or the website that can be accessed. Another problem is some references were not published in English. As this paper would be published in an international journal, I would suggest that the author should cite references published in English.



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4797

Title: Is the validation of biocides against the hepatitis B virus by the use of surrogates possible?

Reviewer code: 00503536

Science editor: Cui, Xue-Mei

Date sent for review: 2013-07-24 14:01

Date reviewed: 2013-08-03 16:48

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript written by Sauerbrei describes a surrogate assay using DHBV culture system for testing the biocide activity for hepatitis virus. Because there is no system analyzing the infectivity of HBV, it could be available as a surrogate analysis. However, the data shown in Table 2 are quite different from the recommendations proposed by WHO as shown below. "Antigenicity and probably infectivity are destroyed after exposure of HBsAg to 0.25% sodium hypochlorite for 3 min. Infectivity is lost after autoclaving at 121°C for 20 min or dry heat treatment at 160°C for 1 h. HBV is inactivated by exposure to sodium hypochlorite (500 mg free chlorine per litre) for 10 min, 2% aqueous glutaraldehyde at room temperature for 5 min, heat treatment at 98°C for 2 min, formaldehyde at 18.5 g/l (5% formalin in water), 70% isopropylalcohol, 80% ethyl alcohol at 11°C for 2 min." The authors must explain the discrepancy between the WHO recommendation and the results shown by the author. In addition, the amounts of serum HBV considerable vary among the HBV-infected patients. Thus, the suitable method for destroying the infectivity of hepatitis virus may be different according to the level of viremia. The authors should discuss on those points.



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4797

Title: Is the validation of biocides against the hepatitis B virus by the use of surrogates possible?

Reviewer code: 00030389

Science editor: Cui, Xue-Mei

Date sent for review: 2013-07-24 14:01

Date reviewed: 2013-09-15 14:37

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The author reviewed the use of system of DHBV and duck embryonic hepatocytes as the method to evaluate disinfectants for efficacy to HBV. The author revised his review article sufficiently according to the reviewers.



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4797

Title: Is the validation of biocides against the hepatitis B virus by the use of surrogates possible?

Reviewer code: 00503509

Science editor: Cui, Xue-Mei

Date sent for review: 2013-07-24 14:01

Date reviewed: 2013-09-18 18:09

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input checked="" type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Dear sir, I read with the utmost attention the manuscript by Andreas Sauerbrei you have kindly sent me last Friday for peer-reviewing. The paper focuses on current methods to assess the efficacy of different compounds which can be used to inactivate HBV. In my opinion the issue is interesting it is also worth of notice how the author paid particular attention topical issue such as ethical and cost-effect aspects of different assessment methodologies. Nevertheless I must say that the paper is not suitable in its present form. My consideration is mainly based on the fact that the paper lack of the appropriate structure required to all peer-reviewed papers published in international journals. In particular in the present paper is a potpourri which mix up a narrative (non-systematic) revision of literature, author's personal view and original data about a new laboratory procedure. In my opinion the paper should have been organized as a methodology report and resubmitted. I would suggest to: A) re-arrange and synthesize the sections "Why to evaluate biocides for their efficacy against hepatitis B virus" and "Methods for testing efficacy of biocides against hepatitis B virus" in order to write a good background/introduction (explain the topicality of the issue concerning your new procedure) B) Expand with in dept description of the procedure the section "In vitro duck hepatitis B virus model for testing virucidal efficacy of biocides" to write the main section of your paper (e.g. description of methodology) C) re-arrange and synthesize the sections "Duck hepatitis B virus as surrogate virus for hepatitis B virus" and "Evaluation of biocides using duck hepatitis B virus" in order to write down your discussion and conclusion section (explain the advantage and limitation of the proposed methodology). In addition I would provide the author 2 additional advice to further improve the paper: A) the bibliography about HBV outbreak is a bit old fashioned, I would not expect to have cited paper of '80s and '90s to describe current way of HBV transmission.



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

In particular: - exposure to dental procedure used to be a way but I would not it is now in high resource setting. -reference 11 (is a paper published in 1992 i.e. more than 20 years ago) it should be change/added with more recent paper (e.g. Bender et al . Outbreak of hepatitis B virus infections associated with assisted monitoring of blood glucose in an assisted living facility-Virginia, 2010. PLoS One.; Lanini S, et al Hospital cluster of HBV infection: molecular evidence of patient-to-patient transmission through lancing device. PLoS One. 2012;7(3):e33122) - reference 12 (is a paper published in 1988 i.e. more than 20 years ago) it should be change/added with more recent paper (e.g. Walsh B et al Outbreak of hepatitis B in an acupuncture clinic. Commun Dis Public Health. 1999 Jun;2(2):137-40) B) the issue of HBV in dialyses must be discussed at the light of the vaccination policies implemented by early '90s for HBV vaccination C) the author should discuss the issue of environmental resistance of HBV D) English must be revised Best



Baishideng Publishing Group Co., Limited

Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 4797

Title: Is the validation of biocides against the hepatitis B virus by the use of surrogates possible?

Reviewer code: 00013065

Science editor: Cui, Xue-Mei

Date sent for review: 2013-07-24 14:01

Date reviewed: 2013-09-19 23:24

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Dr. Sauerbrei has presented an interesting review article in which he aimed to review different systems including surrogate models, especially DHBV cell culture systems, to validate the efficacy of biocides against HBV. There are some limitations which should be addressed. Comments 1) Page 11, ff. The detailed and very long description of a method to prepare a DHBV cell culture system is not necessary. This paragraph could be extremely shortened or deleted. 2) Page 5, 2nd para; the author wrote from chemical biocides, but didn't specify them. 3) Fig.1. What exactly is shown in this figure? A more detailed description is missing. 4) Fig. 2 is totally out of focus. Please present a figure with enhanced contrast and quality. Also the description of the figure is poor, e.g., which antibodies were used? 5) In my opinion a comparative discussion of the different methods (HBV and DHBV) for the evaluation of biocides against HBV would be helpful for the reader. Furthermore, a comparative discussion of the denoted biocides (Table 2) used against HBV would help the reader not to stand alone with unexplained information. 6) Why does the author favour the in vitro DHBV tests as this system is hard to establish for a non-HBV laboratory? **Minor comment:** The English grammar and spelling needs attention at places and should be checked carefully. A number of sentences are much too long.