GSK Comments on Medsafe Consultation: CMN Form B

Overall Comment

GlaxoSmithKline (GSK) welcomes the opportunity to comment on the Medsafe consultation for CMN Form B.

Overall, GSK is supportive of changes proposed to the CMN Form B, as it provides further clarity with regards to the appropriate change categories applicable for CMN applications. Additionally, the proposed changes will help to reduce the number of queries that Medsafe evaluators receive from the sponsor when there is doubt as to which category to select.

For some of the proposed changes, GSK seeks further clarity from Medsafe to avoid any confusion for sponsors when completing the form. GSK has also provided additional suggestions for improvements and revisions to the CMN Form B for Medsafe's consideration.

Specific Comments to the proposed changes

Proposed changes	**GSK comments**
• Change of category name from 'Bulk Active methods of manufacture' to 'Active Ingredient methods of manufacture -Grade 1'. • Addition of 'Grade 2' to the existing category 'Active ingredient method of manufacture.	• GSK supports the proposed category name change. • GSK supports the addition of 'Grade 2' to the existing category 'Active ingredient method of manufacture'. With regards to the 'change in room for cell substrate preparation activities', further clarity is sought from Medsafe as to whether only changes in rooms for cell substrate preparation activities are required to be submitted, or if room changes more broadly should be submitted to Medsafe.
• Introduction of a Self-assessable change notification (SACN) category 'Active ingredient method of manufacture - Grade 3' (fee $360)	• GSK supports the addition of the SACN category for active ingredient method of manufacture changes, as currently there is no category for this type of change and sponsors are required to pay a higher fee for lower impact changes.
• Removal of the category 'Change in site of lyophilisation' (fee $1440). • Inclusion of a change in lyophilisation site under the category 'Finished product manufacturing site' (fee $2880)	• GSK supports the removal of the category 'Change in site of lyophilisation' and the inclusion of this change under the category 'Finished product manufacturing site'

• Removal of the category 'Revalidation of the lyophilisation process' (fee $1440).	• GSK supports the removal of the category 'Revalidation of the lyophilisation process', as this type of change can be captured under existing categories in the form.
• Introduction of the category 'Finished Product Testing site' (fee $1440).	• GSK supports the addition of this new category. Further clarification is sought from Medsafe regarding the implementation of 'additional' test methods which are previously approved.
• Revision of the criteria for 'Finished Product manufacturing process - Grade 3' (fee $720).	• GSK acknowledges Medsafe's clarification on the applicable changes under this category. However, GSK considers the 'change from a single product to a multi-product manufacturing facility' to be quite broad, and wishes to seek further clarity from Medsafe regarding this change (i.e. Do sponsors only notify Medsafe if the manufacturing process of a product changes as a result of a change in manufacturing facility? If there is a change from a single to multi-product manufacturing facility, but no change to the manufacturing process, is a submission to Medsafe required?).
• Introduction of the SACN category 'Finished Product manufacturing process - Grade 4' (fee $360).	• GSK supports the addition of the SACN category for finished product manufacturing process changes, as currently sponsors are required to pay a higher fee for lower impact changes.
• Editorial changes to criteria listed under the various 'Test methods and specifications' categories/grades.	• GSK wishes to seek clarification from Medsafe regarding the second point under 'Test methods and specifications – Grade 3', as this change is unclear: o *change to secondary standard used in assessment of potency/assay, if no protocol for use of a self assessable change for introduction of a new secondary standard has been previously approved.* GSK suggests the following wording: o *change to secondary standard used in assessment of potency/assay, if no protocol has been previously approved.* • GSK wishes to highlight to Medsafe that some formatting changes are required with regards to text that is bold and/or unbold.
• Introduction of categories for 'Excipient specifications/test methods'.	• GSK supports the addition of categories specific to excipient specifications and/or test methods. • With regards to applicable changes under the category 'Excipient specifications/test methods - Grade 1', GSK is of the understanding that if there are changes to the specifications/test methods resulting from a change to a different pharmacopoeia (e.g. USP to BP), a submission to Medsafe is required under this category. However, further clarification is sought from Medsafe with regards to whether a submission is required if there are changes to the specifications/test methods resulting from an update to the

	latest version of a pharmacopoeia.
• Introduction of the category 'Shelf life/Storage conditions - Reference standard used for potency/assay'	• GSK proposes that all changes regarding reference standards are included under the category 'Test methods and specifications'.

Additional suggestions and proposed improvements

GSK would like to take this opportunity to provide additional suggestions for improvements and revisions to the CMN Form B for Medsafe's consideration.

CMN Form B Section	GSK comments
Section 1: Product Details	GSK suggests simplification of Section 1. Currently a separate Section 1 is required to be completed for each product included in the application. This could be simplified by having a table in this section, where sponsors can include the relevant information for each product licence included in the application. This would also significantly reduce the length of the form where multiple products are included in the application.
	GSK requests clarity with regards to why the sponsor is required to specify if the product is currently available and the date of last supply in the form. Can this be removed?
Section 2: Applicant and Sponsor details and declaration	Similar to the requirements for CMN Form A, GSK suggests that Section 2 only be required once for each application, as opposed to per product included in the application.
Section 3: Proposed changes	GSK suggests further improvements are made to the current descriptions for proposed changes, to help sponsors easily identify the appropriate change and application type. GSK's suggestions are provided below: <u>Indications/dosage</u> • Clarity around the need for separate changes for a new indication and modified indication (i.e. is adding a new paediatric population a new indication or a modified indication?). Given both are evaluated under section 24(5), and the same data is required to be submitted, it is unclear why these two indication changes are separate. <u>Data sheet – miscellaneous changes</u> • The description of this change could also include other changes which can be submitted under this category such as expansion to interactions and safety information e.g. adding new interactions, new available pregnancy data, clinical trials updates etc.
Section 4: Summary of	GSK suggests that the section summarising the current and

proposed changes	proposed details be simplified. For example, the reason for the change and consequential changes are captured in the data package submitted by the sponsor. In light of this, GSK questions whether the information is also required in the form. With regards to the field 'acceptance overseas', GSK wishes to seek clarification from Medsafe as to whether this information is required for all CMN types or only specific types. GSK understands that this is useful information to evaluators for CMNs submitted under section 24(5), but perhaps not as relevant for routine CMC CMNs. In addition, GSK notes a typographical error in the summary of current and proposed details table. The table heading should be updated to read 'Proposed product details' to align with the 'Current product details' heading.
Section 5: Declarations and Commitments	GSK suggests simplifying the information in Section 3 Labelling (similar to Section 4 Declaration to accompany a Data Sheet submitted for approval) by including check boxes next to each of the different declarations.
Section 6: Other products affected	GSK suggests Section 6 be deleted given the information is captured in Section 1.
	GSK notes that the requirement for a copy of the current product database report has been reinstated. Could Medsafe please clarify the rationale for this requirement?
General comments	To improve useability of the form please consider: - Inserting section breaks at the end of each section, so that each section appears on a new page - Checking the style/format throughout the form - Upgrading the Microsoft Word document from a .doc file to .docx file, the latter being a more current version. In addition, the current CMN Form B is well structured and it is generally easy to navigate throughout the document. Retaining the ability to delete the change types/tables, which are not applicable to the application, is a positive and GSK would like to request that this feature be retained in the updated form.

We thank Medsafe for providing GSK with the opportunity to participate in this important consultation process.

– End –