7th November 2012

Consumer Healthcare
82 Hughes Avenue
Locked Bag 3
Ermington NSW 2115
Australia

Tel. 61 2 9684 0888
Fax. 61 2 9684 1018

OTC Medicines Regulatory Process Review
Therapeutic Goods Administration
PO Box 100
WODEN ACT 2606
AUSTRALIA

Sent by e-mail:
OTCBPRconsultationpaper@tga.gov.au

Manager Product Regulation
Medsafe, Ministry of Health
PO Box 5013
WELLINGTON 6011
NEW ZEALAND

Sent by e-mail:
medsafeapplications@medsafe.govt.nz

Dear Madam / Sir,

Re: Over-the-Counter (OTC) Medicines Business Process Reform Consultation Paper (Version 1.0 September 2012)

GlaxoSmithKline Consumer Healthcare (GSK) is a global research-based over-the-counter (OTC) pharmaceutical division of the synonymous pharmaceutical company. GSK manufactures and markets a wide range of OTC medicines that are sold in pharmacies and supermarkets throughout Australia and New Zealand. As such, we have an extensive number of registered medicines appearing on the databases of both regulatory agencies, and also routinely undertake a significant number new registration and variation submissions each year.

As an active member of the regulatory community GSK have participated on the OTC BBR Working Group which has met with the regulatory agencies on a number of occasions to provide guidance, comment and insights into the business reform process. Consequently, GSK is well placed to provide comment on the subject consultation paper.

The comments within this document represent the specific views of GSK Consumer Healthcare. They are intended to reinforce and enhance the consolidated industry views that have been outlined in the separate ASMI and NZSMI submissions.

We appreciate the opportunity to make comment on the consultation paper and sincerely hope that our comments are taken in the constructive manner in which they are intended, so as to assist in developing a speedier and transparent OTC product application process.

[redacted]

TGA / Medsafe: Over-the-Counter (OTC) Medicines Business Process Reform Consultation Paper

Consultation Response Submission
Prepared by GlaxoSmithKline Consumer Healthcare

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Executive Summary

- GSK, in principle, is supportive of the OTC Business Process Reform (OTC BPR) provided that the development of the new process results in a process that significantly improves registration timings (particularly of complex registrations), provides predictable outcomes and promotes agency transparency throughout the application process.

- GSK has concerns that some of the processes currently enjoyed in New Zealand under Medsafe and the results achieved, will become slower and less reliable under the new process.

- GSK has a fundamental concern that the OTC process for registration of products has the potential to become as detailed as prescription applications particularly in the area of pre-screening with a higher risk of the loss of the application/evaluation fee.

- GSK has a real concern that the difference in culture and operation between the TGA and Medsafe and the individual regulators' underlying understanding of the implications of the implementation of the new revised process has not been fully appreciated by each other.

- GSK questions the value of the OTC Medicine Monograph (OMM) application process. Based our understanding it is the sponsors of these 'monograph' medicines that occupy a disproportionate amount of agency time and resource to evaluate simply because of the poor quality of the applications, hence to give these same sponsors a 'free ride' via the OMM system (where only assurances rather than data are provided) would appear to run counter to a risk-based approach to regulation.

- GSK does not believe the time allowed before the proposed date of introduction in April 2013 is sufficient to ensure all support materials are available and have been tested by industry to determine if they are fit for purpose. If there is a delay in the release of these support materials and/or they are insufficiently tested they will negatively impact the ability of sponsors to achieve timely and predictable registration outcomes, and for the agencies in delays in processing applications under the new system, resulting in confusion on both sides and potentially otherwise unnecessary rejection of application and lost application fees. We would suggest that the start date be the subject of a separate negotiation that reflects specific milestones being achieved rather than working back from a fixed aspirational date based on unproven assumptions.

- GSK is concerned that there seems to be a 'disconnect' between TGA and Industry concerning the surety of timelines for approval. GSK routinely achieves or betters the TGA target timelines for new applications and changed medicines (except for complex applications), hence we would see the proposed commitment to meet 80% of applications in a certain timeframe as a significantly retrograde step which is counter to the key objectives of the OTC BPR project.

- The Consultation Paper appears to lack true reform with regard complex applications (N4, N5 and C4), other than the freeing of resource by streaming of applications by risk category. In GSK's view the current processes adequately deal with simple applications, it is the processing of complex applications that occupy significant time and therefore most urgently require reform. GSK requests that the TGA and Medsafe should, in collaboration with sponsors, develop novel processes to more effectively process and evaluate complex applications.

- GSK believes that the issues surrounding umbrella branding warrant particular attention. Whilst GSK endorses the objective of avoiding possible harm which may result from

confusing different medicines, we suggest that this is an area of considerable tension between regulators and sponsors, particularly as differences in outcomes for the same product are evident between the tow regulators. GSK therefore encourage the TGA and Medsafe to work as a matter of urgency with Industry to develop practical and relevant and evidence-based guidelines to assist both sponsors and evaluators in relation to umbrella branding (and the related topics of look-alike sound-alike products and indication specific branding).

- GSK believes the requirement for applications to be available in electronic CTD format to be unacceptable in the timeframe proposed. Few sponsors have the necessary information technology in place locally to provide eCTD/NeeS format applications. In any event testing between the regulator and the sponsor would be required to avoid unnecessary errors and delays.

To aid the agencies' review of the GSK response we have set out our comments below in accordance with the page numbering and content structure of the OTC BPR Consultation Paper.

Introduction

In principle, GSK strongly agree with, and support, the need for OTC Medicine Evaluation process reforms. These are clearly necessary such as to provide industry with:

- Predictability of process and timing,
- Clarity of the requirements for application, and
- Transparency of the process and its progress.

Fundamentally the measurement of success against these objectives will be manifested in reduced registration timelines, particularly for complex applications which are the types of applications that are of critical importance to a research-based company such as GSK.

Critical to the success of the project is the availability of crystal clear guidelines, checklists, forms and validated IT solutions. These need to be in place and tested within a suitable timeframe prior to commencement of the new process to allow the industry to familiarise and commence preparation of dossiers and submissions to meet the potentially more exacting requirements. GSK strongly urge the agencies to ensure that the necessary documentation and e-application portal are available at least 4 - 6 months prior to the commencement of the new process. Preparation and lodgement of an application is a significant piece of work. The preparation or review of the product dossier is typically conducted concurrently with the drafting of the application and depending on the complexity, can take up to 6 months or more to complete. The start of the product lifecycle, the product planning and development is already complete at this stage and so any new or vaguely described regulatory requirement will not have been incorporated in the planning. Unless implementation of the new process is carefully managed there is a risk that sponsors will be forced into a position of having to seek remedies such as the right of review according to Section 60 of the Australia Therapeutic Goods Act. Such actions would be costly in terms of time and resources for all parties involved.

GSK recognise the importance of identifying foreseeable issues during concept, planning and development of the process prior to its commencement. Equally at the post introduction stage, the new process will require vigilance for issues that require process adjustment. We are therefore committed to support and collaborate with the TGA/Medsafe through the entirety of the project until the planned benefits are realised.

GSK appreciate that a Risk Management approach should underpin the risk classification of application categories. However, it is clear to GSK, from essentially identical registration applications presented in parallel to both agencies, that each agency has a different approach to risk classification. In GSK's view an approach that involves the use of accepted international practices is better placed to meet the objectives of the OTC BPR rather one which involves creating onerous hybrid amalgamations of the most stringent practices of local and overseas regulatory jurisdictions. It is our hope that GSK's specific comments set out below will help guide the refinement of the new process toward the objectives and scope set out on page 8 of the consultation paper.

Review of the Consultation Paper

Page 3: About the TGA / Medsafe

We note the differences between the TGA and Medsafe descriptions:

1. The TGA has a strong risk focus.

2. Medsafe also includes a focus on efficiency measured against key performance indicators, minimisation of cost of regulatory action, and acknowledges accepted international best practice as a key component of its policy mandate.

We would encourage that both agencies embrace **"accepted international best practice**" as a principle rather than look to create hybrid regional practices that potentially put at risk the viability of Industry.

Page 8: Objectives and scope of the OTC medicines business process review project:

- **Deliver more efficient and cost effective OTC medicines evaluation processes.**

  GSK has concerns that the new process will result in increasing fees to resource more onerous processes, when a more pragmatic approach to regulation that simplifies regulation might be better placed to achieve the OTC BPR objectives. Much time and effort have already been diverted in the last year by Industry and regulators alike in reviewing options for OTC BPR which during some periods have negatively impacted on the processing of applications. This consequential impact reflects on the complexity of the process proposed and may in the end prove simply to be a different process rather than a more efficient and cost effective one.

- **Define application requirements, business processes and target times for applications in each application risk category.**

  The question that arises out of this statement is what will be the circumstances and timeframes as to how the data requirements between the two agencies will be harmonised. GSK has concerns that there has been little consultation on this matter, and the informal indications are that Australian approach will be the dominant one. We believe this to be unacceptable if it proves to be the case. Greater clarity and consultation on this point is required before new harmonised guidelines come in under ANZTPA by 2016.

- **Require applications to be in the common technical document (CTD) format.**

  During the public forums it became apparent that the TGA's intent for electronic submission of dossiers in CTD format is in fact for Non eCTD electronic Submissions (NeeS). At this stage provision of CTD in PDF or word format via email or on CD is within the immediate reach of the majority of sponsors. Provision of the CTD in NeeS will not always be possible, even for multinational OTC medicine sponsors such as us. Unlike the prescription medicines sector where products are predominantly centrally supported, many OTC products are only locally available and few sponsors would have the necessary software within their Australian offices to provide their data packages in the NeeS format.

GSK also request clarity of the actual expectation for the OTC BPR as the expectation for NeeS has only been raised during the public forums, but not in the consultation paper.

Furthermore, is the CTD format to be mandated for both new applications and applications to change existing medicines? This particularly a concern for those medicines which were never originally submitted in CTD format as to do so would require considerable effort for little benefit. None this has not been discussed in the consultation paper.

With regard to the specific modules that constitute a CTD application we would highlight the following in relation to specific modules:

Module 1

GSK noted that during the public forums the TGA confirmed that an OTC Specific Module 1 will be developed as part of the project.

Module 2

It appears that a complete Module 2 will be required for a category N5 application, and will be required as applicable for category N4. GSK look forward to the specific details of the CTD Module requirements being fully elucidated in the revised ARGOM/NZRGM documents that are meant to be in place ahead of the revised process.

Page 9: Phased implementation of the new business processes

GSK has concerns with the vague nature of the phased implementation and the costs associated with implementation of any new process. The TGA would be prudent to take account of the manner in which consultations are undertaken by other like government agencies such as Food Standards Australia New Zealand, where the CRIS often forms part the proposals to be considered.

Additionally, we do not believe the scope of the project as outlined in the consultation document is truly reflective of all the topics under consideration. Information on availability of key items such as: useable Umbrella Branding guidelines and data requirements are poorly described yet the consultation paper and discussions with the agencies indicate that implementation from April 2013 is proposed. This leaves little time for the development of quality forms and guidelines and the training of sponsors in their implementation.

Pages 14 - 15: Changed medicine Applications

- **The applications relating to some quality changes…**
  GSK has concerns with this point as this will move a current legislated New Zealand 45 day application to 120 days evaluation and our understanding was that this was not the intent of the revised process. It might be a better outcome if Medsafe CMNs for all quality changes that are currently C4 should be C2 to align with the table on page 14 and with the proposed categories in Australia. We also seek clarity that sponsors will continue to be able to submit a single CMN for identical changes where a product has multiple classifications registered, i.e. Prescription and OTC together.

General questions:

- **Do you support the concept of risk based categories for OTC medicines?**
  Yes, GSK does support this concept.

- **Do you agree with the proposed risk categories for new medicines?**
  Yes, GSK does generally support the proposed risk categories for new medicines. See GSK responses to Pages 27 – 30 of the Consultation Paper below.

- **Do you agree with the proposed risk categories for changed medicines?**
  No, GSK has concerns with the risk level categories for changed medicines. See GSK responses to Pages 31 – 34 of the Consultation Paper below.

Pages 16 - 19: Proposed OTC medicines evaluation process

Page 16:

- **Applications will be screened by the regulator upon receipt.**
  GSK needs clarity around what the screening process will involve. Whilst GSK agree that early identification of ineffective applications saves all parties a lot time and resource. It would be useful to ensure that the same checklists are maintained for TGA and Sponsors so we are always working to the same expectations. Some form of right of appeal process should be mandated. No specific timeframe is given for this screening process and this needs to be defined.

  The Lodgement and Preparation
  As mentioned earlier, crystal clear support materials will be essential to the success of the reforms (given the significant consequences for sponsors who submit ineffective applications).

Page 17:

- **Application screening phase**
  It is important to maintain a pragmatic approach to application screening and make contact for a simple query without forfeiting fee or returning applications.

  The current guidelines allow for justifications to be included in applications in relation to the omission of safety and efficacy data as well as justifications in relation to literature search strategies. In the public forums, attendees were advised that such justifications would not be assessed for suitability at the technical screening stage. As this level of detail is not suitable discussion at a pre submission meeting to gauge acceptability, the earliest the sponsor will be advised will be at the first Request for Information (RFI). If the justification is unsuitable then both the application fee and the evaluation fee (together with a lot of time and resource) will be lost. It is therefore important that the guidelines are as clear as possible in relation to when a justification can be used as well as the elements of a successful justification.

  As mentioned above, there should be provision at screening to correct administrative oversights within a short period.

  GSK suggests that a letter (possibly automatically generated) should be issued to the sponsor after the submission passes screening to identify the timeframes for each of the stages – this will allow the sponsor to plan resources. In the public forums held in October, the TGA indicated there would be an allowance of a short timeframe for sponsors to address suspected administrative omissions at the screening stage. This was suggested as 48 hours but GSK request that this be 1 week (7 calendar days) thus making reasonable allowances for part time staff, or an absence from the office.

Communication should preferably be by electronic means to ensure out of office responses can be addressed.

GSK has concerns that the two part screening process may include more than just an administrative and technical check of the contents and that elements of evaluation might be incorporated. Any such evaluation will impact on TGA resources. Another concern would be the adverse impact on timelines and predictability if mini-evaluations occur prior to acceptance.

Further detail is required as to what will happen if post-screening the evaluator deems the application to be of a different level of risk than that assigned by the sponsor and accepted at screening.

- **Payment and fees**

  The consultation paper explains that fees will be made payable upon receipt of application and where an application is deficient the application fee will be forfeited.

  At the public forums it was suggested that the application fee will be paid at submission and the evaluation fee will be paid once the application is accepted for evaluation.

  This differs from the current process but will be beneficial to both the TGA and sponsors. It will avoid the need for the TGA to refund evaluation fees and allow Regulatory functions within Sponsors greater control of budget funds and reduce the administrative negotiation for refund.

  GSK looks forward to further detail on the cost recovery model for each of the categories.

Page 18:

- **Evaluation and review phase**

  Request for Information (RFIs)

  GSK is pleased the OTC BPR process allows for up to two RFIs. Clarity of the intent of a question will be critical with RFIs. If there is ambiguity of the evaluator's intent the sponsor's RFI opportunity may be wasted. The existing opportunity for the sponsor to have access to clarify issues with the evaluator is expected to be important to response timeframes and quick resolution of deficiencies.

  It is important that the first RFI is provided with the evaluator's report and includes a single consolidated list of deficiencies sent in accordance with section 31. Where a second RFI is required it should not introduce new questions but should only request information not addressed to the satisfaction of the evaluator from the first RFI.

  It is unclear how the evaluator will proceed to decision where either the timeline for the response expires or where there is a matter still unresolved after two RFIs. The available options to close out the application may vary dependent on risk. They would include; sponsor withdrawal, rejection of the application, approval of the application with conditions or with different details to those requested in the application. In most cases, approval with conditions or different details will be preferable to withdrawal or rejection and the revised processes should therefore reflect this. While an ARTG entry with conditions different to those requested may require a variation to the entry prior to a viable launch of the product, it may involve lower fees, shorter timelines and fewer resources than those for reapplying for a new product application.

No New information

Sponsors require greater clarity of the decision process that will occur regarding whether or not the sponsor is able to submit additional information. Whilst there are examples that have been answered in the public forums, like additional stability time points, there are many examples particularly for complex applications where we believe the sponsor could not have anticipated questions and where items like additional tests may be requested which will require validation, or where a name may be considered unsupported after evaluation of the data.

GSK also request clarification of whether sponsors could make use of the protocol for Shelf life extension and whether this will be allowable under the rule for No New Information.

Applications requiring evaluation by Expert Committees

It is unclear from the consultation document how the process of referral of an application to the Expert Advisory Committee such as ACNM or MAAC will fit into the evaluation and decision process. We would seek clarity around this matter. Clarity of the intent of a question will be critical if the RFI timeline is to be met. GSK would anticipate that with the 1st RFI (which should include the full list of questions) the sponsor would be notified of the issues referred to the Expert advisory Committee and given the opportunity to address the issues to the committee. Whilst the consultation paper identifies that only 3% to 4% of applications are referred to the Expert Committees, this detail is critical to a research-based company such as GSK as more often than not the complex applications that we are involved in that find there way to Expert Committees. *The accessibility of the evaluator is expected to be important to the success of the new process.*

We also highlight our long standing concerns regarding the reduced number of ACNM meetings that have been held each year and the implications to predictability for Industry.

Process Details

While this consultation is on the process framework proposal, there is a need for greater levels of detail of the elements of the proposal to provide more certainty for stakeholders. Detail of what an OMM will look like, greater detail of CTD format, including what "as applicable" means and what parts are actually required, etc. The lack of this type of detail makes it difficult for the industry to envisage the process and how it will work to generate the anticipated benefits.
While ASMI agrees in principle with the reform project it must be noted that at this stage much of the fine detail is still to be developed.

GMP Clearance and expiry

During the OTC BPR Public forums the TGA advised that submissions would need to be made with sufficient expiry remaining on the GMP Clearance of the manufacturers. The rationale for this approach could not be addressed in this forum, but it seemed disproportionate with risk. It will be difficult for sponsors to manage for manufacturers already in MIS particularly where re-audit by TGA is required to be arranged. Existing products on the register at times require extension to the GMP clearance to accommodate clearance updates. Update to the clearance should be able to be accepted by the evaluator at any time during the process. It cannot be considered as 'new information' it is a check box only. The BPR WG will need to have meetings with

the OMQ to work through the detail of GMP Clearance to dovetail with the OTC BPR Process.

Sponsor Communication with Evaluators

The continuing availability of informal pre-submission meetings should be made clear.

We understand from the Consultation Paper that while there will be greater clarity of requirement in the guidance materials; there will also be scope for discussion with the TGA prior to submission. In the public forums this was confirmed but it was advised that communication will need to be structured for efficiency. It was advised that TGA's order of preference was for communication in writing with a written reply, then via a prearranged teleconference and lastly face to face meeting. Further information will be necessary on the structure of pre-submission communication. It was also noted that the requirement for pre submission meetings should be the exception rather than the rule. Should it become a regular requirement the TGA suggested that it may point to a gap or a lack of clarity in the guidance which needs addressing.
ASMI suggests that open communication between the sponsor and the regulator (or evaluator) is desirable (at all stages of the process) and that such dialogue improves efficiency and allows greater clarity of requirement with fewer ambiguities.

General questions:

- **Do you support the proposed five phase process?**
  Yes, GSK supports this.

- **Do you agree with the principles that were applied when developing the proposed process?**
  We agree only in part. GSK would refer to our specific comments above in answering this question.

Pages 20 - 21: **OTC medicine monographs**

- **OTC medicine monographs (OMM)**

At this stage GSK perceives category N2, OMMs, to be of limited value under the current proposal. We suggest that the TGA resource saving is over stated and does not account for Post Market Monitoring Activities (PMM). The TGA advised that the initial 6 OMMs have been prioritized based both on the medicine's suitability and its likely frequency of use. The frequency of use has been based on frequency of applications in the last 2 years. This assessment did not consider whether there were umbrella branding elements to the applications. Further we understand from the public forums that for N4 or N5 applications where the quality module of the medicine N2 (OMM), there will be no risk based approach where an abbreviated Module 3 Data requirement would be applied. We believe this not only limits the applicability of the N2 category to far less than the estimated 15% of applications, but is inconsistent with risk based principles. Where the product strictly adheres to a monograph, other than umbrella branding, or a new indication, the abbreviated module 3 should apply along with the additional data necessary to support the elements that create risk in the application.

As a significant manufacturer of analgesics we would suggest the frequency of applications for Paracetamol/Codeine (one of the proposed 6 Monographs) should be reconsidered with this combination up-scheduled to S3, there is very limited opportunity for market growth of this medicine.

The content of the OMMs and the OMM guideline is as yet unseen. We understand from the public forums that:

- the OMMs drafted during the proposal development will be further refined for ease of maintenance.
- the criteria for resourcing the establishment of a new OMM will be prioritised based on the likely frequency of use based on history of applications.
- the OMMs will contain the specifics of dosage form, strength, indications, labelling and advisory statements and chemistry explaining the pharmacopoeial monograph required.
- the General Guidance for application of OMMs will contain relevant Therapeutic Goods Orders applicable, GMP requirements, acceptance specifications for fragrances/flavours, label submission requirements and a list of assurances.
- Full compliance with a monograph will be required to be eligible for the N2 pathway.
- In labelling 'Words to the effect' will apply for RASML Statements but the wording of indications should strictly adhere to the monograph due to the expectation the assessment will be conducted by staff with some technical skills but not an evaluator.
- Label graphics which make/imply claims will not be allowed. Graphics of dose forms or an age appropriate child would apparently be acceptable for an N2 application. Graphics of body parts or a clock would apparently be considered claim related and not acceptable. This would likewise apply to N1 or clone applications. ASMI suggests that this aspect of the OMMs requires clarification.

GSK is concerned that the lack of flexibility with regards label claims and graphics is inconsistent with a risk based approach and will have potentially significant impact on consumers and on the use by sponsors of the OMM pathway. If words to the effect are allowable for warnings then it is difficult to see the increased risk to consumers associated with the same approach being taken in relation to label claims. If all OMM products are required to have uniform text and graphics then this will prevent differentiation of product and lead to consumer confusion. Additionally, if all OMM products are required to have uniform text and graphics then the OMM pathway will be less attractive to sponsors and will result in fewer products taking this path and therefore the anticipated resource benefits of OMMs will not be realised.

The TGA's proposal provides no detail on Post Market Monitoring (PMM) for N2 applications. At the Public forums it was advised PMM would include targeted and random auditing of N2 applications, where the module 3 data would be required to be provided within a yet to be defined period. PMM would also involve sampling and testing of products. There are also discussions with OMQ to assure quality of these products at audit. Given the points (above) it seems that there will be very few applications based on the OMM. It is questionable if such low volumes justify the establishment of a PMM program.

Questions were asked at the public forum whether products approved via category N2 will require a statement to the effect "this product has not been evaluated for chemistry" on a Certificate of Pharmaceutical Product (CPP) for export. While not previously considered it was anticipated that there would be no impact, but there was a commitment to take this up with the export unit.

- **Cost of Monographs**
  We anticipate that the submission fee for a monograph product will reduce under ANZTPA because less evaluation resource will be required.

- **How do Monographs get updated?**
  Clarification is required around the intended process going forward.

General questions about the proposal to develop monographs:

- **Do you support the concept of developing monographs for some OTC medicines?**
  Yes, but not in the restrictive form described in the consultation paper.

- **Do you agree with the proposed list of medicines that should be given priority for monograph development?**
  GSK has concerns that processes (and criteria) for adding substances to the list of monograph candidates need to be refined. The lack of clarity of this criteria means that the appropriateness of the proposed list cannot be properly assessed.

Pages 22 and 23: Application categorisation for umbrella branded medicines

- **Umbrella branding**

  GSK believes that the issues surrounding umbrella branding warrant particular attention. Whilst GSK fully endorses the objective of avoiding possible harm which may result from confusing different medicines, we suggest that this is an area of considerable tension between regulators and sponsors. GSK therefore encourage the TGA and Medsafe to develop relevant and evidence-based guidelines to assist both sponsors and evaluators in relation to umbrella branding (and the related topics of look-alike sound-alike products and indication specific branding).

  This is a complex and multi-faceted area. Branding and brand recognition through brand extension ("umbrella branding") are key issues for OTC medicines, both from an industry viability perspective but equally importantly from the consumer self-selection perspective. The costs associated with establishing a novel non-prescription medicine brand (as well as developing consumer awareness and trust) are considerable. These costs will be a key determinant in the decision to launch a new product. Inappropriate restrictions on umbrella branding will have a detrimental impact on access to new products.

Pages 24 – 26: Target times

- **Process and timeline proposals**

  Target Timeframes

  Neither TGA target timelines (nor the Aspirational timelines) provide a proposed timeline for the two part Screening process. For predictability of the process from end to end GSK request that this needs to be defined, measured and reported. Without transparency of this part of the process there is potential for a queue to develop just as it has in the present system.

  In the public forums held in October, the TGA indicated there would be an allowance of a short timeframe for sponsors to address suspected administrative omissions at the screening stage. This was suggested as 48 hours but GSK request that this be 1 week (7 calendar days) thus making reasonable allowances for part time staff, or an absence

from the office. Communication should preferably be by electronic means to ensure out of office responses can be addressed.

There is an apparent unevenness in consequences for not meeting the proposed timeframes of the new process. Where a sponsor misses a deadline in a response, the application 'may' proceed to decision and risk rejection or forced withdrawal. On the other hand, where the TGA misses an average target timeline there will be no consequence.

Instead the TGA/Medsafe commit to meeting the target timelines for 80% of applications in each category. When considered that this means 1 in 5 applications will be outside the target timeframes for each category, which seems at face value less than predictable. GSK recommend that whilst working to reduce timeframes to the 2016 Aspirational timeframes, TGA/Medsafe should not lose sight of the key objective of predictability.

Another concern is that there appears to be no transparency to allow one to determine whether an application will fall outside the target timeframe until it happens. The 1 in 5 applications outside target timeframes should be reviewed as part of a continuous improvement process, understanding the causes for the delays and taking action to address them. GSK recommend that TGA/Medsafe should also set an aspirational percentage continuum that ensures that continuous improvements are made. Ideally GSK would like to be in a position by 2016 to see move to mandatory timelines.

Finalisation, appears to be outside the quoted TGA target timelines, but appears to be included in the Aspirational timelines. GSK understood from responses to questions in the public forums that this stage is administrative only and should be similar to current to current experience, i.e. not long.

We also note that both the Aspirational and TGA target timeframes are presented in calendar days, rather than the TGA OTC Section's tradition working days. We question how part time evaluators will deal with meeting the timeframes.

Sponsor timelines

The detail on Sponsor timelines in the consultation was confusing. Clarification was given in the public forums and we now understand that the Aspirational timelines provide sponsor response times related to the Medsafe legislated timeframes. However for Australian sponsors the requirement Under Section 31 of the Act states timeframes for response must be 'reasonable'. GSK understand the evaluator's preference for the shortest reasonable timeline for response to ensure the evaluation detail is still within recall. GSK have reviewed past applications and to attempt to categorise them to the new framework and look at identifying standard response times for each category. The reality of establishing standard acceptable timeframes by category of application is less straight forward. In practice situations differ based on type of questions and situation of sponsor to obtain responses. These timeframes can be affected by criteria such as where the product is being sourced and therefore result in differences regardless of the category of application. GSK therefore believe the current S31 requirement for "reasonable timeframes" remains appropriate. It would assist sponsors if at commencement of evaluation the evaluator could provide a non-binding advice as to when questions can be expected to allow sponsor companies the best opportunity to ensure resources are available in a timely manner. GSK also propose that at the receipt of the RFI letter sponsors confirm to commit to a response timeline (e.g. 30, 60, 90 or 120 days).

Reform of Complex applications (Category N4, N5 and C4)

The BPR process appears to lack true reform with regard complex applications (N4, N5 and C4). Other than suggestions that the OMM process and streaming of applications by risk category will free up resource, little detail of how this will be achieved has been provided. There appears to be a lack of review of the issues causing the current timeframes associated with complex applications. There needs to be a greater understanding why issues arise whether it is a lack of clarity or absence of guidelines and/or subjectivity around umbrella branding and what really poses risk to the consumer.

For example one of the key impediments to having applications evaluated is the waiting time for clinical data to be assigned to external evaluators. Periods in the region of 12-14 months have not been uncommon before external evaluators are allocated to a particular application. In other instances external evaluations have been put aside and additional evaluations undertaken, further unnecessarily lengthening the approval process. Clearly freeing up TGA resources will not resolve such situations.

GSK is concerned because there is a lack of transparency of what guidelines TGA are applying and what they may reference. Even where industry work to available guidelines and to Therapeutic Goods Orders our current experience indicates TGA have the power to arbitrarily draw on other sources and introduce additional requirements.

In the main complex applications are made by multinational companies, the supporting data in dossiers are prepared for global submission and products are intended for global supply. These same applications are often quickly approved by Medsafe and other like jurisdictions, yet Australian specific requirements e.g. addition of test methods, different finished product specifications, different labelling, concerns about the efficacy all seem to find their way into TGA evaluations. All these unique requirements add significantly to lengthening the approval process as well as to the cost of goods, which ultimately the Australian consumer pays.

Pages 27 – 30: **Risk Categorisation Framework for New Medicine Applications**

GSK is in general agreement with the consultation as to the risk level categories for new products.

However, there is uncertainty about the extent to which these risk level categories have been subjected to testing with real world examples. GSK suggests that the categories need to be subjected to challenge with real world examples.

For the sake of clarity of requirements (e.g. in relation to category N4), statements such as “”as required” and “as applicable” should be replaced with unambiguous statements such as “quality data will only be required for those products that are in category N4 as a result of their inclusion in Appendix X”.

Pages 31 – 34: **Risk Categorisation Framework for Changed Medicine Applications**

The format in the Consultation Paper used to present the change categories is not user friendly. GSK requests that the presentation in the current ARGOM be retained (i.e. a table listing changes by attribute of the product being changed, with additional columns to indicate change category). This would allow for the additional useful

guidance on what is not considered a regulatory change (i.e. current change category "O"). This would also allow for identification the changes which result in a separate and distinct good (i.e. a new product application).

Notifications

GSK is disappointed at the apparent removal of the current category "N" changes. These low-risk changes can currently be made by way of notification, whereby the TGA is informed of the change at the time the sponsor implements the change (i.e. there is no need to wait for the TGA to approve the change before implementing it). The TGA has suggested that such changes are incompatible with the *Therapeutic Goods Act* and that all changes must be approved by the TGA prior to implementation.

Given that the Consultation Paper indicates that 70% of current variations are notifications, if all notifications now require prior approval then this represents a significant step backwards and will inevitable tie up more resources at the TGA.

GSK at no stage has been made aware that there is any evidence of increased risk or failure associated with the current system of notifications. Indeed, notifications have been part of the TGA system since its inception.

GSK also notes that overseas jurisdictions (e.g. NZ, UK, Canada) all allow changes by way of notification or self-assessment.

GSK is concerned that the ability to make changes by way of notification will be lost as part of the OTC BPR Project and suggests that if the current legislation does not allow notifications, then the legislation needs to be amended.

Risk Classification – Variations

There is general agreement as to the risk level categories for new products.

There is concern that the risk level categories for variations have not been subjected to a close review and that the risk level categories for variations have not been subjected to testing with real world examples.

As discussed above, there is concern that changes by way of notification will no longer be available to sponsors under the revised processes. (This becomes even more important if the OTC reforms result in increased numbers of post-approval variations – also see above).

GSK would also highlight that it is unclear what levels of data will be required to be submitted for variations in general.

Concluding Comments

Reform Timing

GSK have significant concerns as to the practicality of the proposed OTC BPR commencement date of April 2013. GSK feel that a critical phase to the commencement of the new process is the readiness of the Industry to use it. This requires the availability of all the support materials (guidelines, monographs, checklists and forms drafted, consulted, and finalised and the IT solutions developed, prototypes tested and ready to go live) with sufficient time to allow for the preparation of new and changed applications in readiness.

Should the support materials only be provided immediately prior to the commencement of the new process a lag-time in the submissions of applications would occur of an estimated 1-6 months based on category of application. For example C1 and N1 applications might be submitted quickly after commencement but the higher risk classification products would take several months to prepare.

Project Plan Visibility

GSK feels that it will be important for industry to have some visibility of the proposed project plan to understand the timing of the:

- Development and consultation on the necessary guidelines, checklists and IT solutions required to provide the fine details of the reforms.
- Cost Recovery Impact Statement consultation for Fees and Charges for the new process.
- Information sessions on the practicalities of the new process and its implementation.

This will build confidence in the sponsor's ability to interact with the new process prior to the implementation.

The OTC BPR working group particularly require project plan visibility to allow for resource planning to ensure they can be available to support the project.

Communications

Further consultation and education prior to commencement of the new process will be essential to the success of the reforms.

In the OTC BPR Working Group meeting which GSK attended it was suggested that there should be two rounds of consultation.

1. Consultation on the proposed reforms (i.e. this consultation)

2. Consultation on the final process detail

GSK believes that there needs to be extensive consultation on the supporting guidelines, forms, checklists etc. However the consultation paper does not make this clear. GSK would also like to see information sessions prior to commencement of the new process, but it is unclear how and when this will all occur prior to commencement in April 2013.

Additionally, a suitable transition period will need to be included to allow sponsors to submit applications that are being developed and finalised now.

Furthermore, communications post-implementation will be essential so as to inform stakeholders as to the progress of the reforms, the performance of the TGA, the performance

of sponsors and to advise on the inevitable changes that result from the program of continuous improvement.

IT Functionality

The planned functionality in OPAL to support the process is not described in the consultation paper.

It had been proposed to the OTC BPR Working Group that there would be on-line tools that would take the user through a decision tree which would identify; the risk category type, the detailed data requirements, the costs and the timings. This data would then form the checklist for administrative screening of the data package required at submission.

The application entry portal (based on the decision tree) was proposed to be available both immediately for submission purposes, as well as for use in the planning of new products and variations to ensure the development of appropriate data packages. This would assist sponsors to understand the relevant parts of the CTD for the OTC submission recognising that not all parts are necessary for all applications.

During the public forums it was made clear that the TGA's IT proposals for the OPAL application forms are intended to provide hints and additional information particular to the application category to assist in providing clarity of the requirement for each application, but it was unclear whether the system would lend itself as a planning tool.
It is unclear if this vision is still planned as a deliverable for the process.

Guidelines, Resources etc

GSK would like to stress that clear and unambiguous support materials will be essential to the success of the reforms.

All the support materials must be available sufficiently in advance of the commencement of the reforms to allow sponsors to prepare effective applications. These support materials should include clear guidelines, monographs, checklists and forms (which need to be drafted, consulted, and finalised) together with IT solutions that have been developed, tested and are ready to go live.

The support materials need to be as clear as possible given the significant consequences for sponsors who submit ineffective applications under the proposed reforms.

Apparent Reform

In GSK view the reforms proposed in the Consultation Paper can be summarised as follows:

- There will be a different approach taken for OTC Medicines than has been taken with prescription medicines.
- There will be a streaming process for applications, based on risk categories.
- There will be different target times for each stream.
- There will be a "monograph" system for well characterised substances.
- CTD format will be mandatory.
- Notifiable changes will no longer be notifiable.
- Post-market surveillance will now be necessary for low risk products.

In summarising the above it becomes apparent that there has been no fundamental, positive, reform to the way in which applications are actually evaluated (other than to stream them). There are no obvious reforms aimed at delivering speed, efficiency, predictability or transparency to Industry.

Whilst GSK has actively participated and supports the regulatory agencies in these first steps at taking a different approach to OTC Medicines registration, we remain to be convinced that the OTC reforms outlined in the OTC Medicine BPR Consultation Paper will result in anything more than simply creating a streamlined process for the assessment for a limited number of well characterised medicines.

To allow for a viable research based OTC environment to exist in Australia and New Zealand any new OTC process must allow Sponsors to bring to market innovative products that meet customer needs. Throughout this consultation process there remain unanswered questions regarding the speedy and transparent processing of complex applications and the ability of companies to extend the brands that are fundamental to their existence with clarity and predicability.

We look forward to working with TGA, Medsafe and our Industry colleagues towards outcomes that address these needs.