Johnson & Johnson Pacific

AUSTRALIA • FIJI • NEW ZEALAND

7th November 2012

Dear Sir / Madam

RE: TGA OVER-THE-COUNTER (OTC) MEDICINES BUSINESS PROCESS REFORM (BPR)

Thank you for the opportunity to provide comment on the TGA Over-the-Counter (OTC) Medicines Business Process reform (BPR). Johnson & Johnson Pacific Pty Ltd (JJP) is a manufacturer and marketer of a wide range of over the counter (OTC) products in Australia and New Zealand. JJP have consulted with both the Australian Self Medication Industry (ASMI) and the New Zealand Self Medication Industry Association (NZSMI) and support the submission provided by both these associations.

Please find attached JJP's response to the TGA Over-the-Counter (OTC) Medicines Business Process reform (BPR). (Version 1.0, September 2012).

Please contact me if you have any queries or require further clarification regarding this submission.

Yours faithfully,

Nadine Saraceno
Regulatory Manager - OTC
Johnson & Johnson Pacific Pty Ltd
Phone: +61 2 8260 8587
Fax: +61 2 8260 8518
Email: nsaracen@its.jnj.com

INTRODUCTION:

JJP supports the Business Process Reforms (BPR) and commends the TGA for developing a model which ensures a more cost efficient and effective evaluation process and that the quality of OTC medicines lodged with the TGA improves, to provide greater clarity, transparency and predictability of timeframes for sponsors, using a risk based approach to ensure the right level of evaluation is applied depending on the type of application.

Key to the success of the BPR is absolute clarity of the requirements and visibility of the proposed project plan including consultation on guidelines and timings for each item. It is critical that the TGA apply consistency (through Standard Operating Procedures or Checklists) with how applications are reviewed from screening to decision, the availability of clear guidelines, checklists, forms and validated IT systems within a suitable timeframe prior to commencement of the BPR, to allow sponsors to familiarise themselves with the requirements and expectations to ensure that dossiers can be submitted that will be accepted for evaluation. Any ambiguity in the guidelines must be addressed ahead of the BPR implementation date to avoid unnecessary confusion and rejection of applications following the evaluation of an application, which will ultimately be beneficial for both industry and TGA/Medsafe. Even upon BPR is implemented it is important that the TGA allow flexibility as there may be unforeseen/exceptional circumstances where the BPR may not be able to be adhered to, and exceptions will need to be considered for the process to remain reasonable and fair. TGA/Medsafe will need to remain open to process improvement and a transitional period upon commencement of the BPR is imperative to allow industry and TGA/Medsafe alike to familiarise themselves with the new process. Given the above points, we believe that the implementation timings of April 2013 is extremely ambitious given the amount that needs to be consulted on, tested and in place, ahead of the BPR implementation date.

Prior to the commencement of the BPR, the application portal needs to be available at least 6 months prior to the commencement of the process as 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 previously misunderstood regulatory requirement will not have been incorporated in the planning.

SPECIFIC ISSUES THAT JJP WOULD LIKE TO RAISE IN RELATION TO THE KEY FEATURES OF THE PROCESS:

- *Applications will be screened by regulator upon receipt*:

  JJP understand that there will be two levels of screening including screening and initial evaluation. JJP would like to understand the difference between the two levels of screening under the BPR versus the current process. For predictability of the process from end to end JJP believe that this needs to be defined, measured and reported thus we believe that target timelines should also be considered for the two part Screening process. Without transparency of this component of the process there is potential for a queue to develop and a true understanding of when an application would be expected to be completed would not be clear.

- *Incomplete applications will not be accepted for evaluation and fees will be forfeited*.

JJP would like more clarity and guidance on what constitutes an incomplete dossier. Currently Sponsors have an opportunity to submit missing information following the screening process, however if the requirements of screening will differ under the BPR, sponsors require more definitive guidelines/checklists of when an application will be deemed unacceptable for evaluation, versus when an application will be accepted for evaluation provided the missing information is supplied within a reasonable number of working days (at the TGA BPR Roadshow 2 working days was suggested however we believe five working days is more reasonable to account for staff members taking holidays, or being sick or working part-time).

- *There will be a maximum of two rounds of requests from the regulator for the applicant to supply additional information.*

  Overall JJP has no objections to this proposal, however we require further clarity on how unresolved issues at the final round of questions can be resolved with the evaluator in order to avoid rejection.

  It is not unusual for OTC products to have unresolved issues, mostly around brand differentiation, brand name/umbrella branding that previously has required a lot of back and forth discussion, both over the phone with the evaluator, as well as through email. Therefore understanding whether there would still be the opportunity to have the informal discussions with the TGA prior to formal response would be greatly appreciated, or details as to what this mechanism should be, as this would ensure transparency, clear communication and expected outcomes for both sponsor and the TGA/Medsafe. It would also avoid unnecessary rejections of applications.

  The BPR consultation also notes that once the sponsor submits an application that they will not be able to make changes or submit additional information, as the Request for Information (RFI) process is not intended to provide sponsors with an opportunity to supply information that should have been included in the original application (unless required to address specific questions). JJP agrees with this principle and expect the same from the TGA. New questions not raised in the first round should not be raised in the second round. This has occurred previously with application number OM-2010-00963-3 where a TGA peer reviewed decision on a product name during a formal RFI to JJP was overturned at a later RFI, and application OM-2010-00621-3 where questions regarding validation were only raised during the 3rd round of questions when they should have been raised at the first round of questions. Thus this principle is important for both Industry and the TGA/Medsafe. The only type of additional information we question that could be included during the evaluation process is additional stability data as supplementary time points may become available during evaluation. This is particularly important for the more complex applications where the application can remain open with the TGA/Medsafe for a number of months.

- *Target timelines will be specified for receipt of company responses to request for additional information*

  There is an apparent unfairness in consequences for 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. Where the TGA misses an average target

timeline there will be no consequence, we encourage that the system allow flexibility under exceptional circumstances (explained below). JJP understands the evaluator's preference for the shortest reasonable timeline for sponsor response, however the reality of establishing standard acceptable timeframes by category of application is less straight forward. In reality situations differ based on type of questions and circumstances including where the product is being sourced from and therefore will differ regardless of the category of application. We therefore believe the current S31 requirement for "reasonable timeframes" remains appropriate. It would also assist if at commencement of evaluation the evaluator could provide non-binding advice as to when questions can be expected to allow companies the best opportunity to ensure resources are available at the expected time of questions. JJP proposes that at the receipt of the RFI letter that sponsors confirm to commit to a response timeline of either 30, 60 or 90 days. This could also allow for exceptional circumstances when unanticipated questions arise that could require additional tests included in the finished product specification which will require development and validation of test methods, thus sponsors could choose a response time that will be appropriate depending on the types of questions received. We also expect that the TGA/Medsafe to accept the additional information under these circumstances given it would be a request by the evaluator, or a consequence of the evaluation report. We trust that this will not result in rejection of an application. A sponsor should be given no less than five working days to make this decision, as it may require discussions with global teams to decide the best plan of action.

The TGA commit to meeting the target timelines for 80% of applications in each category. Medsafe are already meeting and exceeding these timeframes therefore it is a step back for NZ based applications. In Australia, when considering that this means 1 in 5 applications will be outside the target timeframes for each category, it is not very predictable. We believe that 90% is more predictable. JJP suggests that if 1 in 10 applications outside target timeframe is not acceptable for the TGA at this stage, then we believe that the TGA should review their metrics as part of a continuous improvement plan, understand the root cause for the delays and take appropriate action to address the delays. JJP also suggests that the TGA should set an aspirational percentage ensuring that continuous improvements are made. JJP would like the TGA to be in a position by 2016 to move to mandatory timelines.

Furthermore, there is no transparency regarding when a sponsor will be advised that their application will fall outside the target timeframe, it is important that the sponsor is made aware before evaluation commences, otherwise the BPR will not provide greater transparency and predictability for that particular sponsor.

SPECIFIC ISSUES THAT JJP WOULD LIKE TO RAISE IN RELATION TO NEW MEDICINES APPLICATIONS AND CHANGED MEDICINE APPLICATIONS:

Categories:

- *N2 OTC Medicine Monographs (OMMs)*
  JJP is concerned that the volume of applications that will go through the OMM stream is not the anticipated 15%, especially if labelling graphics (<u>not</u> specifically umbrella branding) is an issue that would force the application to a higher stream, as discussed at the Melbourne TGA BPR roadshows. We suggest that the TGA be more specific with what constitutes true umbrella branding, opposed to new graphics or line extensions which do not have an umbrella branding

component, as currently it is confusing for sponsors. We suggest that the TGA resource saving is over stated and does not account for Post Market Monitoring Activities (PMM). The TGA advice that the initial six OMMs have been prioritised based both on the medicine's suitability and its likely frequency of use based on the applications received over the last 2 years, did not consider whether there were graphics/branding elements that would require evaluation at a higher stream. Furthermore, we understand from the TGA BPR Roadshows that for N4 or N5 applications where the quality module of the medicine is equivalent to N2 (OMM), that there will be no risk based approach by TGA/Medsafe where an abbreviated Module 3 data requirement would be applied (equivalent to N2). We believe that this further limits the applicability of the N2 category and is inconsistent with risk based principles of the BPR. We believe that where the product strictly adheres to a monograph, other than umbrella branding or a new indication that the abbreviated module 3 data requirements should apply, along with the additional data necessary to support the elements that create the higher risk in the application. This approach is far more aligned with the risk based principles.

The content of the OMMs and the OMM guideline is yet to be seen. For a sponsor to assess the suitability of an OMM, the requirements need to be captured under the Quality Standards which will control the quality of the product registered under this system. These Quality Standards will need to be specific and comprehensive in order for them to effectively control the product without oversight from the TGA. JJP is also concerned that processes for updating monographs has not been clarified, nor has the process for the creation of additional monographs. Furthermore, we are concerned that the original list of OMM's presented at the OTC BPR Working group has been greatly reduced. We would suggest that all effort be made by the TGA to re-instate the original list.

There is uncertainty around the flexibility of the monograph system such as how "fast" type claims supported by dissolution would fit within the monograph system, whether words to the effect would be considered acceptable, and whether a sponsor has the option of choosing one or all of the indications listed in the monograph. In order to apply the risk based principles, we believe that flexibility in this regard will be required as the TGA/Medsafe should only review the element of the application that presents a risk and openness to the above should be considered.

The TGA's proposal provides no detail on Post Market Monitoring (PMM) for N2 applications. At the TGA BPR Roadshows 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.

<u>Complex Applications:</u>

The BPR process 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 which is questioned. There appears to be a lack of review of the issues causing the current timeframes associated with complex applications and we fail to see how the BPR will address these issues. There is also a large concern that the risk of a costly complex application submitted through the BPR has a much higher chance of being rejected than with the current process, therefore we ask the TGA/Medsafe to be mindful of this before the implementation of the BPR. The issues would be mostly due to ambiguity of guidelines and the concerns that could be raised by an evaluator

during the evaluation process, especially when there will be no opportunity for sponsors to submit additional data during the RFI stage, and the limitation to two rounds of questions. As an example, a complex application can be submitted with a complete data pack in line with the ARGOM requirements as certain sections ie: in the Safety and Efficacy Chapter allows for circumstances where safety or efficacy can be justified, thus actual efficacy or safety clinical studies are not required. If the sponsor chooses to justify, it will rightfully pass all levels of screening and evaluation will take place. However what would the end result be if the TGA deemed the justification unacceptable? The sponsor has followed all the correct processes and paid all the fees. Additional data could not be submitted at this point in time given the BPR will not allow for this, and a pre-meeting would not address this as review of the data would not have taken place. This leaves the sponsor in a very difficult position. JJP would really encourage TGA/Medsafe to consider these circumstances and the high risk it presents for industry. A specific example we would like to bring to the TGA's attention is application OM-2010-00621-3. This application was subject to a TGA pre-meeting and based on ARGOM it was accepted that JJP could submit the application without an efficacy clinical study. However during the evaluation process the external evaluator raised potential abuse issues which were not raised in any other market where this application was submitted that could only be addressed by submitting "additional" documentation. This application was eventually approved, however under the BPR this application would likely face rejection at no fault of the sponsor. This highlights the lack of reform in this particular area and we urge the TGA/Medsafe to think of these types of applications and allow flexibility under exceptional circumstances as these applications are highly resource intensive and very costly.

It is also unclear how the Advisory Committee of Non-prescription Medicines (ACNM) will fit into the Evaluation and decision process and how it will affect the TGA target timelines. JJP believes that in most cases referral to the ACNM would occur after the RFI (it would not be known at the time of acceptance of submission). The sponsor would be notified of the issues referred to the ACNM and given the opportunity to address the issues to the committee, however how will this additional step affect target timelines, especially when timings will depend on the next available ACNM meeting. While the consultation paper identifies that only 3% to 4% of applications are referred to the expert committees, the absence of detail as to how the ACNM will fit into the new process is concerning as it is evident that this aspect of the evaluation process has not been considered as part of the BPR.

SPECIFIC ISSUES WITH THE PROPOSED FORMAT OF THE CATEGORIES OF APPLICATIONS:

- New Medicine applications

The risk category framework is not in a very positive language and has the potential to cause confusion, as in some circumstances it is a process of elimination to determine the stream an application will fall under. TGA/Medsafe will also need to be mindful that the categories may have the potential to be a little bit simplistic and in some circumstances it may not fall into a specific stream. We urge the TGA to trial the categories will real life examples.

We also believe that there is some ambiguity in terms of the requirements. In relation to category N4, statements such as "as required" and "as applicable" these should be replaced with unambiguous statements which make it clear exactly what is required. In addition, the "notes" in the table is too confusing and does not facilitate the interpretation.

The BPR working group had also discussed and agreed that where an application would otherwise comply with the OMM apart from either an umbrella brand name (N4) or a new claim or indication (N5), the application should require an abbreviated Module 3 data package for the N2 application plus the additional data requirements to justify name/claim/indication. This may be implied in the Appendix 1 tables in the wording "Complete Module (except where ARGOM/NZRGM specifies that a complete module is not required)" but is not confirmed in the text of the consultation. In the public forums the TGA indicated that categories N4 and N5 would require the submission of the complete Module 3 and that only N2 applications would be able to use the abbreviated data package. JJP is quite concerned that there has been a change in position in relation to this.

- Changed Medicine Notifications

Current format in the proposal is not user friendly. JJP believes that it would be a lot simpler if the existing table in ARGOM was maintained, with additional columns to indicate change category. This format is already familiar to sponsors and user friendly, this will also allow the maintenance of what is not considered a regulatory change ie "O" changes.

JJP is disappointed with the removal of the Notification "N" category in the risk categorisation framework for changed medicines applications and replaced with the C1 category which has a target timeframe of 28 days and requires full evaluation. Currently, Notifications are a self assessable stream, whereby the TGA is informed of the change at the time the sponsor implements the change. 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.

JJP is concerned that TGA are not following the risk based principles in this regard as it is proposing the removal of a "Notifiable" category which has been working effectively for many years with no evidence of increased risk. Applying full evaluation for this category is unnecessarily and not aligned with the risk based principles. This is also particularly concerning given 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 restrict resources at the TGA further.

We also note that this is out of step with New Zealand, whereby Medsafe allows for self-assessable changes, - the change being considered effective from the date of payment.

Electronic CTD:

During the public forums it became apparent that the TGA's intent for electronic submission of dossiers in CTD format is in fact for NeeS. Currently JJP can support an electronic CTD in pdf or word format via email or on CD, however NeeS will not always be possible especially when applications are in relation to locally manufactured products, thus NeeS format cannot always be supported. JJP believe a searchable pdf or word document should be sufficient for the TGA thus we request clarity of the actual expectation for the OTC BPR, as this has not been elaborated on in the consultation.

Umbrella branding:

JJP acknowledge that this is a very complex area which requires special attention and care. It is important for the TGA to be clear that applications with a low risk umbrella branding segment do not require evaluation at a higher stream, and that branded products with/without graphics should not require a higher level of evaluation.

JJP suggests that this area requires more in depth exploration and consultation with all stakeholders to generate confidence that reforms will achieve the stated objectives and not result in unintended consequences. It is important that sponsors are clear on the stream an application is required to go down based on the labelling. The TGA in collaboration with consumers, industry and other stakeholders should pursue the development of clear guidelines and protocols which would assist both sponsors and the TGA to objectively assess the risks associated with product brands, names and packaging.

CONCLUSION:

In conclusion, JJP agrees in principle with the objectives and scope of the OTC medicines BPR review project and agree wholly with the risk based principles applied to the evaluation of OTC medicines. However, there are areas within this consultation that present concern to JJP which we would like addressed.

The process still lacks the clarity that is required to ensure an unambiguous, fair and robust process. It is imperative that clear guidelines (including umbrella branding guidelines), checklists, forms and validated IT solutions are available within a suitable timeframe prior to commencement of the BPR, therefore implementation timing of April 2013 is unrealistic.

Target timelines do not take into account the screening phase, which we believe should be included for the purposes of predictability to sponsors. In addition we believe that 90% of applications should be completed within each stream.

The proposal lacks true reform in some areas and the risk based approach is not always applied, in fact in the case of Notifications they have become unnecessarily more stringent and the issues surrounding complex applications have not been addressed, nor how the ACNM will be incorporated into the target timelines. Furthermore, it is not clear why an otherwise N2 stream application with an umbrella branding component cannot be submitted with an abbreviated Module 3 data package given this component does not present any risk, this further highlights the inconsistency with the risk based principles and requires further attention. For the future success of the BPR, flexibility when circumstances are encountered which may require review of an application outside of the strict BPR should also be considered to ensure fairness in these situations.

The monograph system requires more clarity and there is uncertainty regarding the flexibility and the requirements of the use of the N2 stream and the future list of OMM is also questionable.

We expect that the TGA will regularly review their metrics as part of a continuous improvement process, understand the cause for the delays and take appropriate action to address the delays, with the aim of mandatory timeframes by 2016.