OTC Medicine BPR Consultation

Response from Ego Pharmaceuticals

November 7, 2012

Introduction

In principle Ego Pharmaceuticals (Ego) agrees with and supports the need for OTC Medicine Business Process Reforms to provide industry with:

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

Fundamental to the success of the reforms is clarity of requirement and rigidity of process to screen out applications which are ineffective prior to significant commitment of TGA resource. Critical to the success of the reforms is the availability of crystal clear guidelines, checklists, forms and validated IT solutions within a suitable timeframe prior to commencement of the new process. This will allow industry sufficient time to become familiar with the new process and to commence preparation of dossiers and submissions to meet the exacting requirements. Ego recommends that the necessary documentation and e-application portal needs to be available at least 6 months prior to the commencement of the 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 previously misunderstood regulatory requirements will not have been incorporated in the planning. Unless implemented carefully there is a risk that sponsors will increasingly seek reviews under section 60 of the *Therapeutic Goods Act*.

Ego understands the importance of identifying foreseeable issues during concept, planning and development of the process prior to its commencement. However it is also important that, post introduction, the new process is monitored for issues that require process adjustment, and opportunities that present for improvement. Implementation of a program of continuous

improvement of the revised processes will be essential to the success of the reforms. We are therefore committed to ongoing collaboration with the TGA and with Medsafe through the entirety of the project until the planned benefits are realised.

Ego supports the Risk Management approach underpinning the risk classification of application categories. We look forward to a consumer focused risk management culture. We also look forward to decision making that clearly articulates where and why deficient applications do not meet the Act, the Regulations or the Guidelines and thereby pose unacceptable risk to consumers. Such articulation will be key to the success of the process, allowing sponsors to learn and to improve the quality of applications and ensuring decisions will withstand scrutiny on review. It will also lead to the continuous improvement of the guidelines to ensure guidance is current and unambiguous.

Ego's major concerns with the proposal are detailed below

Reform Timing

Ego has significant concerns at the practicality of the proposed OTC BPR commencement date of April 2013. Ego suggests that critical 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 with sufficient time to allow for the preparation of new and changed applications in readiness for the new process. It is suggested that these support materials will 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. Should the support materials only be provided immediately prior to the commencement of the new process then a lag-time in the submission of applications will occur of an estimated 1-6 months based on category (i.e. complexity) of application. For example C1 and N1 applications might be submitted quickly after commencement but the higher risk classification products (i.e. more complex applications) would take months to prepare.

Project Plan Visibility

Ego suggests 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 BPR working group particularly require project plan visibility to allow for resource planning ensuring 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.

Ego has previously 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

Ego still believes that there needs to be consultation on the supporting guidelines, forms, checklists etc. However the consultation paper does not make this clear. Industry 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

Ego would like to stress that crystal clear 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.

Ego suggests that these support materials will 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

Ego suggests that 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 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.

Ego is concerned 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 efficiency, predictability, transparency.

While Ego supports the TGA for taking a different approach to OTC Medicines, we suggest that OTC reforms ought to include more than simply streaming the different types of applications.

Complex Applications

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. 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 of why issues arise whether it is lack of clarity or absence of guidelines and/or subjectivity around umbrella branding and what really poses risk to the consumer. Industry is concerned because there is a lack of transparency of what TGA are applying and what they may reference. Even where industry works to published guidelines and Therapeutic Goods Orders, our current experience indicates that TGA evaluators still draw on other sources to introduce additional requirements.

Ego understands that the current processes adequately deal with simple applications and that it is the processing of complex applications that occupy significant time and therefore most urgently require reform.

Ego suggests that the TGA and Medsafe should, in collaboration with sponsors, develop novel processes to more effectively process and evaluate complex applications. Ego also suggests that it is not sufficient to say that streaming and the use of monographs will free up resources to deal with complex applications.

Timelines Generally

Ego supports the assignment of different timelines based on the category of application. Ego is concerned that the TGA's target and aspirational timelines will not be to be backed up by

mandatory (i.e. legislated) timeframes and that an 80% target will be applied (see further discussion below).

Ego suggests that there needs to be a benchmarking exercise conducted before the reforms commence in order to accurately measure the effectiveness of the reforms.

Ego notes that Prescription Medicines in Australia have mandatory (i.e. legislated) timeframes. We suggest that the mandatory timeframes for Prescription Medicines may lead to TGA resources being drawn towards processing prescription applications (with mandatory timeframes) at the expense of OTC applications (which only have target timeframes).

Ego is concerned that sponsors will be penalised if they don't meet the required timeframes, but that no such penalty will apply to the TGA if the timeframes are not met.

Ego also notes that overseas jurisdictions have mandatory timeframes for OTC medicines (some with penalties for failing to meet those timeframes).

For these reasons, Ego suggests that the having mandatory timeframes to back up the target timeframes is essential and should be one of the longer term aims of the reforms.

TGA Timelines

Neither the TGA aspirational nor the target timelines include proposed timelines for the two part screening process. For predictability of the process from end to end, Ego believes these need to be defined, measured and reported. Without transparency of this part of the process there is potential for a queue to develop.

There is an apparent asymmetry 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. The TGA and 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 it sounds less predictable. Ego suggest that while working to reduce timeframes to the 2016 aspirational timeframes, the TGA and Medsafe should not lose sight of the goal of predictability, and remember that it was

of greater importance to industry than the timeline itself. There is no transparency to know whether your 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. Ego suggests that the TGA and Medsafe should also set an aspirational percentage (at least 90%) to ensure that continuous improvements are made. Ego suggests that one of the longer term aims of the reforms should be the adoption of mandatory TGA timeframes for all applications by 2016.

Finalisation, also appears to be outside the quoted TGA target timelines, but appears to be included in the aspirational timelines. Ego understood from responses to questions in the public forums that this stage was administrative only and should be very brief (consistent with current experience). Nevertheless, timelines for this part of the process should be included in the total timelines (as should the screening times).

We question whether the Advisory Committee process will be outside the target timeframes. We also note the reduced number of Committee meetings held this year and the likely impact on predictability for industry.

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 were based on sponsor response times related to the Medsafe legislated timeframes. However for Australian sponsors the requirement under section 31 of the Act is that timeframes for response be reasonable. Ego understands the evaluator's preference for the shortest possible timeline for response to ensure the evaluation detail is still within easy recall. Ego reviewed past applications and attempted to categorise them against the new framework and looked at identifying standard response times for each category. The reality of establishing standard acceptable timeframes by category of application is less straight forward. In reality situations will differ based on the type of questions, the sponsor's resources, the type of product, the site of manufacture and not simply the category of application. Ego therefore believes the current S31 requirement for "reasonable" timeframes remains appropriate. It would assist sponsors if at commencement of evaluation the evaluator could provide advice as to when questions can be expected to allow sponsor companies the best opportunity to ensure resources are available

in a timely manner. Ego also proposes that at the receipt of the RFI letter sponsors confirm their commitment to a response timeline (e.g. 30, 60 or 90 days).

In the public forums 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 Ego suggests that one week might be more suitable so as to allow for part time staff, or an absence from the office. Communication should preferably be electronic to ensure out of office responses can be addressed. Ego notes that one week would still not be long enough for sponsors to actually generate missing data (and so would still only allow provision of material left out through oversight).

Process

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).

Screening

Ego agrees that early identification of ineffective applications saves all parties time and resource. It would be useful to ensure that the same checklists are available for both the TGA and Sponsors so that both parties are always working to the same expectations.

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.

Ego 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.

Ego is concerned 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.

Request for Information (RFIs)

Ego 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. While 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 claim may be considered unsupported after evaluation of the data.

It is questioned 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.

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 Ego agrees in principle with the reform project it must be noted that at this stage much of the finer 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 requirements 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.

Ego 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.

Umbrella Branding

Ego suggests that the issues surrounding umbrella branding warrant particular attention. While Ego 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.

We 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.

Consistent with a risk-based approach, proposals should be reflective of the risks posed by the different categories of products. For example, the potential risks associated with ingesting a medicine are different from those associated with topical application of product.

Furthermore, Ego 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. 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.

Additionally, Ego believes that evidence-based and objective decision-making would be greatly enhanced by the development of a broadly acceptable label testing methodology. The aim of such a methodology would be to generate test results that would provide confidence that any risks in relation to product identification and other issues impacting on safe use have been effectively addressed.

Ego proposes that the TGA commissions a paper on international best practices for label comprehension testing. Ego remains available to work with the TGA to develop appropriate guidelines and protocols.

New Medicine Applications

Framework

There is general agreement 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. Ego 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”.

Category N1 Explanatory Notes in Appendix 1 indicates the "Parent product must have been fully evaluated (safety, efficacy and quality)". While it is noted that this is consistent with the ARGOM 03 wording for clones "The ‘parent’ product must have been fully evaluated (ie. not a grandfathered product)" Ego believe that the proposed terminology is too restrictive. For example this would apparently mean that a parent product containing Phenylephrine/Analgesic combination would not be eligible to be cloned.

The BPR working group had also discussed, and agreed, that where an application would otherwise comply with the OTC medicine monograph apart from either an umbrella brand name (N4) or a new claim or indication (N5), the application should require for Module 3 the abbreviated data package for the N2 application plus the additional data requirements to justify name/claim/indication etc. 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. Ego require further discussion and confirmation.

<u>OTC Medicine Monographs (OMMs) - Generally</u>

Ego is concerned that the monograph system will only apply to 15% of new product applications and that the anticipated efficiencies will not be attained. This will be compounded by the level of TGA resources expended on post-market surveillance of monograph products.

Ego is concerned that processes for updating monographs have not been identified in the Consultation Paper (and nor have processes for adding additional monographs).

There is uncertainty as to how other allowable claims (e.g. “fast”) would fit within the monograph system. It has been suggested that these sorts of claims might have to be

incorporated by way of variation post-approval. Such an increase in the workload of sponsors and evaluators is not in keeping with the stated aims of the reforms.

Ego repeats suggestions made by the OTC BPR Working Group that the term “monograph” be abandoned. This term will create unnecessary confusion because it is already used to describe pharmacopoeial items as well as regulatory constructs of other agencies (all of which are already familiar to sponsors and regulators alike).

At this stage Ego 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 advise that the initial 6 OMMs have been prioritised 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 should a medicine, that would otherwise comply with an OMM, be classified as N4 or N5 (because of the proposed product name and/or indications) then the abbreviated Module 3 data requirements associated with the OMM will not 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.

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

- the OMM’s 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. Ego suggests that this aspect of the OMM's requires clarification.

Ego suggest that the lack of flexibility with regards to label claims and graphics is inconsistent with a risk based approach and will have potentially significant impacts 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. Will such low volumes justify the establishment of a PMM program?

Questions were asked at the public forum regarding 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.

OTC Medicine Monographs (OMMs) - Candidates

Ego is concerned that an initial list of OMM candidates presented to the OTC BPR Working Group has been substantially reduced. Ego understands that the list was shortened on the basis of TGA resources (as opposed to the risks associated with the products).

Ego suggests that the original list be re-instated and that the items on the list be *prioritised* based on TGA resources rather than *omitted*.

For reference, the initial list was as follows:

- Cough/cold products
- Sinus/allergy/sinus pain products (not including cetirizine or loratadine)
- Combination analgesics
- Aspirin
- Ibuprofen
- Paracetamol
- Pholcodine
- Pseudoephedrine hydrochloride
- Doxylamine succinate
- Dextromethorphan hydrobromide
- Guaiphenesin
- Loperamide hydrochloride
- Mebendazole
- Ranitidine hydrochloride
- Nasal decongestant sprays/drops
- Antiseptic and Anaesthetic Lozenges
- Topical antifungals
- Topical Anaesthetics / Analgesics / Antipruritics

Ego suggests that processes (and criteria) for adding new substances to the list of monograph candidates need to be defined. The absence of this criteria means that the appropriateness of the proposed current list(s) cannot be properly assessed.

Ego suggests that inclusion on the list be based on risks to the consumer (and not based on risks to the regulator). Ego also suggests that inclusion on the list should reflect an objective assessment of those risks and should be unrelated to the workload of the regulator.

Changed Medicine Applications

Framework

The format in the Consultation Paper used to present the change categories is not user friendly. Ego suggests 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).

Ego 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.

Ego is concerned 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.

Ego notes that there is no 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. Ego also notes that overseas jurisdictions (e.g. NZ, UK, Canada) all allow changes by way of notification or self-assessment.

Ego is concerned that the ability to make changes by way of notification will be lost as part of the 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, but 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.

Ego notes that it is unclear what levels of data will be required to be submitted for variations in general.

Section 25

Ego suggests that the impact of the proposed reforms on the operation section 25 of the *Therapeutic Goods Act* needs to be more fully examined. Under section 25 the evaluator needs to be satisfied that the quality, safety and efficacy of the goods have been established. In the past this has led some evaluators to go beyond the requirements of the TGOs or the Guidelines and reference additional requirements that the sponsor could not have reasonably anticipated. This is of concern under the proposed reforms for two reasons; firstly such an approach will disadvantage sponsors who will now have limited opportunity to justify and no opportunity to submit new data; secondly will evaluators be able to satisfy themselves if they are bound by the clear published guidelines necessary for the proposed reforms?

Advisory Committees

It is unclear how the ACNM or MAAC will fit into the Evaluation and decision process. Ego would anticipate that with the first RFI (comprehensive 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. While the consultation paper identifies that only 3% to

4% of applications are referred to the expert committees, this detail is critical to sponsors. The absence of detail as to how the advisory committees will fit into the new process is concerning for two reasons; firstly it makes it difficult to provide useful feedback; secondly it is evidence that this aspect of the evaluation process has not been considered as part of the reforms.

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 format will not always be possible even for multinational OTC medicine sponsors. Not all sponsors have the necessary software within their Australian offices and many local contract manufacturers are unable to provide their data packages in the NeeS format. Ego requests clarity of the actual expectation for the OTC BPR given those proposals for NeeS have only been raised during the recent public forums.

Ego was pleased that during the public forums the TGA confirmed that an OTC Specific Module 1 will be developed as part of the project. Ego also looks forward to the details of the requirements for CTD Modules 2 and 3 being fully explained in the revised ARGOM/NZRGM.

Fees and CRIS

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 sponsor's greater control of budget funds and reduce the administrative negotiation for refund.

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