Consumer Healthcare Products Australia

Consumer Healthcare Products Australia
ABN 55 082 798 952
Suite 1, Level 2
35 Chandos Street
St Leonards NSW 2065
+61 2 9922 5111
PO Box 209, St Leonards NSW 1590

info@chpaustralia.com au
www.chpaustralia.com au

24 February 2021

[redacted]
Scientific Evaluation Branch
Australian Government Department of Health
PO Box 100,
Woden ACT 2606
[redacted] tganames@tga.gov.au

Re: Removing redundant processes for entering certain formulation information into a therapeutic goods application

CHP Australia provided preliminary feedback to this proposal last year as part of the scoping discussion to inform this consultation paper (See attachment A). We note that there has been no substantive additional information provided in the public consultation paper to addresses our concerns. The proprietary ingredients system has been widely acknowledged as serving a useful purpose for industry and the TGA, however there are a number of areas that could benefit from improvement. It is therefore disappointing to see that the improvements we have requested are being overlooked in favour of implementing some process changes that appear to have little to no benefit to industry, and their overall benefit to the TGA is difficult to rationalise in relation to the industry burden they will introduce. Our key issues remain as follows:

- We are disappointed that this is the extent of the reform to the Proprietary Ingredient System, given previous discussions with the TGA.
- We question the issue or need that is driving this change. Other than advice that these *"administrative processes associated with three categories of Proprietary Ingredients mixtures were identified as redundant and resource intensive or did not fit within the broader purpose of the TGA's proprietary ingredient system."*

  The main driver for this activity is to limit the Proprietary Ingredient notification process to mixtures that only contain excipient ingredients. No changes to existing legislation or IT systems would be required to implement this proposal.
- We need greater detail of TGA's plans for how they would implement this change. While this may represent a simple administrative change for TGA, this consultation paper has provided insufficient clarity of how the TGA plan to implement this proposal. There is still little clarity of exactly how industry would

transition – apart from these PIs would no longer be available to include in new applications.

- We question the lack of clarity of transition arrangements to allow for time to implement and to consider how the impact of the costs of the change can be minimised. The current paper indicates that for Active Premixes transition will be considered on a case-by-case basis but without provision of criteria that might determine that basis. We are concerned about areas for which significant cost and time burden could be created by this proposal including regulatory costs to apply for new replacement products, GMP change implications, and impact on exported medicines and CLPs/CPPs. This consultation paper does not demonstrate that TGA have understood the cost implications of the proposal to industry, just to continue to market their existing products.

While clearly presented as a deregulation initiative, with a graphic of cutting red tape on the front cover of the consultation paper, the reduction of regulatory burden is hard to fathom:

- Ingredient suppliers would now be required to repeatedly provide that proprietary information to every sponsor who requests it, rather than just providing the information once to TGA.
- Ingredient suppliers for some product types would now need to provide sponsors/finished product manufacturers with a quantitative formula, not just the qualitative information.
- Instead of one standardised TGA form, different sponsors may request the information in different formats to meet their internal system requirements thereby increasing the amount of work and complexity for suppliers in providing the information.
- Sponsors applying for new products would now have to enter multiple ingredients for every product that uses that premixed ingredient instead of entering one proprietary ingredient into a medicine application.
- Sponsors applying for new products containing herbal extracts will now need to accurately enter complex extraction information into the ARTG for each application instead of entering one proprietary ingredient, which has been notified by a supplier with an in-depth understanding of the extraction process.

For both sponsors and ingredient suppliers this will increase the amount of work needed to be done. It increases both the complexity of ensuring the ARTG information is correctly and consistently entered, and the chance of error. For example, entering the details of herbal extracts in an application for a new listed medicine can be complex. The Proprietary Ingredient (PI) system makes that process easier and

prevents errors. If the active herbal extract PI is removed there is increased risk of errors and some sponsors may not be able to correctly interpret what steps of the herbal extraction process do or do not need to be included in the ARTG. This introduces potentially additional regulatory costs if assistance from regulatory consultants is needed to get the entry correct or if listings and labels need to be updated to correct errors. While many sponsors do manage this aspect of listings confidently, the broad range of sponsors in the listed medicines market mean that having this simplification of process is invaluable for some sponsors.

Members report no issues with the time it takes TGA to get new PIs onto the Proprietary Ingredients Table. When developing a new product there is typically plenty of time to request the ingredient supplier to submit the PI notification to the TGA and have the PI included and available well before the product application is required to be submitted. Feedback from members is that the PI system, with its existing scope is helpful and does not represent a regulatory burden, although there are aspects of the system that would benefit from improvement. The PI system performs a useful function and reduces complexity and red tape for industry and ingredient suppliers. Removing it would remove a one-off activity for each PI for the TGA but would create more confusion in understanding ARTG records and comparing them to manufacturing formulations. And this also would increase workload and red tape overall for both industry and suppliers.

CHP Australia is unable to support the proposals in their current form. The lack of details to reflect how the flow-on regulatory burden of these changes can be managed and mitigated represents a substantial cost and time burden to industry and applies a narrow lens to a complex issue. During this consultation process there has been a lack of acknowledgement of the very real impact that removing this administrative process for this subset of ingredients will have on industry, with the proposals focussing on streamlining one aspect of the system instead of seeking to improve the efficiency of the overall PIs processes.

Finally, it is not clear why consultations are being managed in such a way that only allows for responses to specific questions, rather than enabling a more fulsome discussion with stakeholders. The removal of the ability to provide a comprehensive response to consultations through the consultation hub reduces the quality of consultations by assuming that the premise for the consultation is correct rather than open to discussion and shuts down the ability to consult on broader principles surrounding a proposal. CHP Australia is very concerned by this approach to consultation becoming the standard.

Please find our responses to the survey questions below and please don't hesitate to contact me for any clarification of the detail provided within the responses.

Kind Regards,

Proposal 1: Discontinue processing of active ingredient mixtures into the Proprietary Ingredients Table

Proposal Details

We propose to cease the processing of new Active Premix and Active Herbal Extract entries into the Proprietary Ingredients Table.

For existing Active Premix and Active Herbal Extract entries, we propose:

- *to inactivate any PI numbers in these categories not linked to current ARTG entries*
- *where an affected PI is used in an active ARTG entry (to be considered case-by-case):*
    - *to allow continued use with no further action or*
    - *to allow sponsors to update their medicine formulations to replace the PI number with the individual constituent ingredients within their ARTG entries. The TGA may consider whether a transition period would be needed for the sponsor to update their ARTG entries.*

For New medicine applications proposing to use an Active Premix or an Active Herbal Extract TGA propose that Sponsors - *will need to obtain relevant formulation details and enter these into their ARTG application instead of selecting a PI mixture. For listed medicines applications, quantities of some excipients are not required to be entered into the electronic system for the medicine to meet listing requirements.*

Do you support the above proposal? Why/why not?

CHP Australia do not support the proposal to discontinue processing of active ingredients mixtures into the Proprietary Ingredients (PIs) Table. Given the TGA has acknowledged the broader practical implications of this change with respect to GMP, it is hard to comprehend why this consultation paper has not provided greater insight into the criteria that will apply for TGA's case-by-case consideration of implementation and the transition arrangements for existing listed and registered medicines.

For context, the TGA is not suggesting that all PIs are removed from the Proprietary Ingredients Table, so the selective nature of this proposal indicates that TGA acknowledge the value of PIs for simplifying information for medicines. It is therefore difficult to understand how this proposal will deliver on the presented objectives to remove redundant processes and address data integrity when PIs will remain part of the system. It is also difficult to rationalise how the cost burden on industry is warranted for these select changes, given the PI mechanisms are otherwise considered beneficial and effective.

Further background to GMP requirements for active premixes

From a GMP perspective it is important to first acknowledge that where an active ingredient requires the presence of an agent to stabilise it for use, that stabilising step is considered as part of the manufacture of the active and not as a step of manufacture of the finished goods.

Registered non-prescription applications are required to provide evidence of GMP for Active Premixes when considered a significant step of manufacture. As such the TGA's online application form, underpinned in legislation, facilitates provision of API Premix Manufacturer's GMP Clearance. So, for a direct compression paracetamol PI, the sponsor must maintain a clearance for the manufacturer of that premixed active. There is a lack of clarity whether this proposal will essentially remove the API manufacturing step, by the need to list all ingredients, and whether this will become harder to differentiate the API from a step in the finished product manufacture. The removal of the Active Premix PI will contribute to confusion within the ARTG as to the manufacturing process.

Listed medicines are not required to provide a TGA Clearance for an Active Premix or for an Active Herbal Extract and the TGA's online application form, underpinned in legislation, makes no provision for nominating API premix manufacturers to the ARTG record. Instead, sponsors (or their finished product manufacturers) are required to satisfy themselves of the equivalence of the GMP applied by the ingredient manufacturer. There are practicalities which have informed this allowance for Listed medicines. This recognises that complementary medicine ingredients are typically not regulated in other countries as pharmaceuticals, but as foods or dietary supplements. This means that TGA's mutual recognition agreements (MRA) with other pharmaceutical regulators do not extend to the MRA regulators conducting inspections of sites not regulated by them in their country. The Australian sponsor would therefore need to pay for TGA to travel and inspect these sites. As foods there are similarly requirements for safety and quality to be controlled and standards met. The ongoing review and qualification of the supplier is also addressed as part of the GMP activities of the finished product manufacturer.

This proposal for active ingredient mixes in listed medicines, where the constituent ingredients of a current PI are now to be detailed into a new ARTG entry, creates a subtle shift in the interpretation for the sponsor/finished product manufacturer which has significant implications. Now the receipt of this premixed active is no longer consistent with the ARTG entry which lists the individual ingredients. Therefore, when the finished product manufacturer receives the premixed active, it may be difficult to be receipted as an ingredient for which a 'GMP waiver' has been provided. Instead, it could now be considered as the active mixed with other individual ingredients of the finished product formula, which have undergone a first step of manufacture, conducted by an entity other than the finished product manufacturer. The relationship

between the finished product manufacturer and the premix supplier potentially changes from that of a 'raw material supplier' to that of a 'outsourced step of manufacture', for which the PI supplier will need to provide a *release for further processing*[1] confirmation to the finished product manufacturer to facilitate release for supply.

To reflect this change in relationship, the sponsor may now interpret this to be a requirement to vary the ARTG entry to include an additional manufacturer, first applying for a GMP clearance for the active premix manufacturer. As noted above, this will typically require an application to TGA to conduct an inspection of the site for TGA certification. GMP Agreements will need to be in place between the sponsor, finished product manufacturer and the active premix manufacturer and local supply agents.

This is a requirement which may be difficult to negotiate with an active premix manufacturer who may comply with cGMP standards for manufacture but may not hold a GMP certificate which lists the final products/goods in question in their scope considering their focus on manufacture of actives. This is a particular concern if they typically don't have direct commercial dealings with the finished product manufacturer due to the relatively small volumes of materials procured for the Australian market.

The cost for TGA GMP certification will become an ongoing requirement approximately every 3 years. While the TGA can share the cost of the inspection between each of the sponsors using that active premix manufacturer, this still represents a substantial and ongoing cost to industry, and may lead to the discontinuation of products due to the increased costs not being viable for ongoing supply.

TGA proposal to inactivate any PI numbers in these categories not linked to current ARTG entries.

This proposal sounds innocuous enough, until you consider that a sponsor may be developing a product containing a PI that is not currently linked to another ARTG entry. That sponsor can't know that PI is not in use in any other products, and under the current proposal, they will only discover this inactivation at some point following the implementation. Whether this is in a Registered medicine under evaluation or a draft Listing application about to be submitted, the proposal fails to recognise the impact of this supposedly small change on the full product lifecycle.

If any such deletions are to occur, CHP Australia would expect that TGA would publicise the list of PI numbers proposed to be deleted, at a suitable period prior to their deletion. This would provide for transparency and allow for sponsors to adjust their new product dossier prior to its planned submission date.

---

[1] Releasing medicines manufactured at multiple sites

CHP Australia would also expect TGA Names to cross-check all components used in PIs proposed for deactivation with the Therapeutic Goods (Permissible Ingredients) Determination. The availability of historical PIs has been demonstrated to be a useful tool for correcting any omissions during the creation of the Permissible Ingredients Determination.

TGA consideration of a transition allowance on a case-by-case basis

The proposal that TGA would allow sponsors to update their medicine formulations to replace the PI number with the individual constituent ingredients within their ARTG entries along with the TGA's consideration of transition on a case-by-case basis, requires much greater clarification:

- How will this be managed? Will sponsors have to prepare a case for each product that is not deemed suitable to continue with a particular PI in the ARTG entry.
- Will this be initiated by the sponsor or the TGA, and how would the sponsor initiate this process?
- How will each case for transition be determined?

The practicalities of managing the impact of removal of Active Premix and Active Herbal Extract PIs on a case-by-case approach for an unknown number of products (based on 793 PIs) is difficult to fathom. To ensure any sort of consistency and predictability for industry in managing these changes the TGA would need to develop internal procedures or protocols. Therefore, if TGA are going to need to develop protocols for managing the transition then it would contribute substantially to transparency for industry if we were to be made aware of what these protocols potentially could be as part of the consultation of the changes.

Ordinarily such a change to an ARTG entry from a single PI to entering a list of other ingredients would render the product 'separate and distinct', requiring a new application to register or list the product, which would result in a new AUST R/L number. It also assumes the PI supplier will provide each sponsor with the quantitative formula.

We have assumed that the TGA can't provide commercial in confidence information belonging to the PI supplier without their permission to provide an automated update of ARTG entries. For example, TGA provide an IT solution to update ARTG entries, such that the PI is exploded to display its constituents and their quantities (when required) within the ARTG entry.

Where the PI supplier is not willing to freely hand out the quantitative formula to Australian sponsors, the sponsors would need to attempt to negotiate confidentiality agreements or to consider reformulation. The timeframe to achieve a confidentiality

agreement cannot be estimated. The cost of reformulation would be a severe penalty to streamline part of a TGA process.

On the assumption the supplier freely provides the formula of the PI, the transition arrangements would need to allow for the following:

- For registered medicines:
    - preparation of a revised dossier and drafting the new online application and uploading of the dossier,
    - payment of application and evaluation fees as well as the timeframe for evaluation and finalisation of the new ARTG entry (~6 - 9 months).
        - This total regulatory timeframe will be upward of 12 months depending on the category of application. This assumes the application is for a (N3/RCM3) generic category of application (~$11,800/~$23,730) and assumes sponsors have resource available to implement this change to simply reinstate an existing product.
    - Once the new AUST R number is available the new label artwork can be finalised to commence printing labels for the manufacture of the 'new' product. Where finished product is manufactured overseas an allowance of sea freight time (8-10 weeks) before the new product could commence supply, replacing the existing product. Of course, detailing of all stakeholders in the distribution chain needs to occur, to avoid confusion and the perception the product is 'new and different'.
    - However, the supply of the 'new' product does not then mean the existing product can be deleted from the ARTG. The sponsor would need to continue to pay annual fees to maintain the existing ARTG entry (with PI) on the register until at least the date of expiry of the last batch of that product released, noting some sponsors with low appetite for risk will have policies to maintain the registration for shelf life + X years. Maintaining the product on the register after supply has ceased is important to underpin that product's ongoing supply and marketing consistent with legislation in some of the States.
- For listed medicines:
    - As indicated above, before an application could be made to update the ARTG, consideration would need to be given as to whether the process would still be considered an API pre-mix or if this is now a step in finished product manufacture requiring GMP certification of the PI supplier. If required, an application would need to be made and certification could take a year or more to receive from the date of application.

- The sponsor's product dossier would need to be amended to reflect the constituent ingredients of the PI and the drafting and submission of the online application form along with payment of the application fees.
- Again, commencement of printing labels and then manufacture of the 'new' product is dependent on receipt of the new AUST L number.
- As for registered medicine, the sponsor would need to pay annual fees to maintain the previous ARTG entry (with PI) on the register until at least the date of expiry of the last batch of product released to support the product's ongoing supply in the market consistent with legislation of some States.

Other practicalities of implementation and potential confusion at post market review

There is a lack of clarity about how duplicate ingredient information will appear in the final ARTG entry, if an excipient is being provided from more than one source. This is likely to lead to confusion for some sponsors if they are to add an ingredient to the ARTG for each time it is added to the formulation, or if it should be added once as a total amount (or with no amount if it an excipient with no restrictions). There is potential for these types of issues to cause confusion at GMP inspection or at a post market compliance review as the ARTG information could appear inconsistent with the Finished Product Specification.

Do you have any other suggestions for managing existing Active Premix and Active Herbal Extract entries in the Proprietary Ingredients Table?

As with any issue the best place to start is to describe the problem statement, and then discuss the details of the issue with key stakeholders to identify possible options to address the issue and the pros and cons of each, before proceeding to propose a solution. This first step in this consultation has been missed. We understand the imperative the digital transformation is creating to optimise and/or streamline the processes prior to them being reflected in the new IT systems. However, this imperative should only heighten the need to work together to find solutions that work for all users of the system. In the absence of understanding the exact nature of the issue, it is difficult to provide other suggestions to manage them.

Ideally, to mitigate the timeframes and the costs of the regulatory requirements of TGA's 'Proposal 1', an automated process that explodes the information of the PI into its constituent ingredients in each affected ARTG entry. This would reflect the administrative nature of the change and reflect that no change to the entry has actually occurred. However, this would still not address the issues that emerge with regard GMP and whether they are appropriate in all instances.

This approach would mitigate the timeframes and the costs of the regulatory requirements we have identified for TGA's 'Proposal 1' in requiring sponsors to reapply for their products. It would require a suitable transition period to allow sponsors to address any changes to provisions for TGA GMP Clearance details for the PI into the ARTG entry. However, this would require TGA to discuss and explore these aspects with the industry before attempting to solve the problem.

Do you have any other suggestions for managing ARTG entries that use the affected PI numbers in their formulations?

Please see above.

[Sponsors] Are there any educational or guidance materials you may need to assist you in entering your product's formulation details into TGA systems?

Different Branches of the TGA appear to have different interpretation of GMP requirements for listed medicines. Greater clarity and consistency of approach to GMP requirements for listed medicines is required.

Proposal 2: Discontinue processing of non-specific Excipient Mixes into the Proprietary Ingredients Table

Proposal Details

For existing Excipient Mix entries in the Proprietary Ingredients Table, we propose:

- *to inactivate any PI numbers in these categories not linked to current ARTG entries*
- *where an affected PI is used in an active ARTG entry (to be considered case-by-case):*
    - *reclassify existing mixtures into other categories. For example, numerous entries in this category include 'moisturising base' in the title, implying that the 'Cream (ointment) base' category would be more appropriate for the mixture. TGA could write to the affected suppliers requesting that they select a more appropriate category, noting that this may affect the mixture's validation in certain TGA application systems.*
    - *allow sponsors to update the formulations of their ARTG entries from the PI number to instead select individual constituent ingredients. In this*

situation, TGA may consider whether a transition period would be needed for the sponsor to update their ARTG entries.

- *Where they [the PI supplier] supply a product that includes ingredients with more than one purpose (e.g. a flavoured capsule shell) they could either:*
    - *submit multiple Proprietary Ingredient notification forms to create separate PI entries in the Table (e.g. one for the capsule shell and one for the flavour component). The sponsor would then select each PI number into their therapeutic goods application; or*
    - *provide details of the constituent ingredients of the mixture to the sponsor (e.g. either the capsule shell component, the flavour component or both) to allow them to individually enter these ingredients into their therapeutic goods application.*

Do you support the above proposal? Why/why not?

Based on the information currently provided on the implementation arrangements and how industry would be assisted through this change, CHP Australia **is not in a position to support** 'Proposal 2'. From a principle's basis, we do not oppose the expectation that an excipient PI should have a clear purpose, and that "non-specific excipient mixes" do not meet this expectation. Ceasing to process new PI notifications for non-specific excipient mixes does not in itself cause a concern for CHP Australia, given the range of specific excipient types, and assuming that any additional categories could be added quite easily due to the administrative nature of the PI notification form. However, the suggested implementation of this proposal, including the case-by-case approach for amending existing ARTG entries, does not provide adequate assurance that the impact on industry is going to be mitigated, during a change to what is essentially a small part of the PIs system.

Under this proposal the PI supplier may choose to resubmit the non-specific excipient premix as one of the specific excipient premixes. CHP Australia have received confirmation from members that those non-specific excipient premixes they currently use would likely fit other specific categories of PI. TGA have not indicated whether they have explored the possibility of facilitating this change from one category to another (except in the case where a PI has more than one purpose), and whether they could or would facilitate the change of category without necessitating a change to the PI number. If this could be achieved, then the impact on updating ARTG entries would be minimised.

The example provided in the consultation paper of a capsule shell mixture that included a flavour mixture, with implications of not triggering vital validation rules within online medicine application portals for flavour or fragrance PIs, indicates a need for greater guidance for PI applicants. The proposal that the PI supplier submit multiple PI notification forms for the one PI, to create separate PI entries in the Table

(e.g. one for the capsule shell and one for the flavour component) and that the sponsor would then select each PI number into their therapeutic goods application, raises several questions:

- Will the two PI entries be linked such that one can't be inadvertently selected without the other?
- Where is the streamlining of process in this proposal?
- Are there no IT solutions to allow for the flagging of those key constituent ingredients that would flag a validation rule? For example, that the PI application form seeks advice of combination category PIs and identifies the presence of ingredients related to each nominated category such that the single PI entry can trigger validation warnings within the product application.

If no facility is to be provided by TGA, then while there would be no actual change to the product, the sponsor would need to apply for a variation to impacted products, a grouping should apply to change from one PI number to the re-categorised PI number (which would negate the need for the AUST R or AUST L number to be changed, hence no label change). However, to affect this change would require application to vary the ARTG entry. For a registered medicine this would attract an application and evaluation fee and for listed medicines an application fee as follows:

Registered OTC Medicines	Application Fee $1680 and an evaluation fee of $4160
Registered Complementary Medicine	Application Fee $770 and an evaluation fee of $4200
Listed Medicines	Application fee of $860

We question whether this was fair and reasonable to reinstate an existing product. If TGA is not able to amend the PI category for the product in the background for the ARTG, CHP Australia would expect to see an extension to the grouping process to allow a change to a PI with a different purpose, a fee waiver for any application and evaluation fees, and a formal transition period to facilitate these updates.

Do you have any other suggestions for managing existing Excipient Mix entries in the Proprietary Ingredients Table?

Please see above.

Do you have any other suggestions for managing ARTG entries that use the affected PI numbers in their formulations?

Please see above.

ATTACHMENT A

Consumer Healthcare Products Australia

20 November 2020

CHP Australia – comments on integrity of data held in TGA systems and specific proprietary ingredient categories

CHP Australia appreciates the opportunity to consider this proposal and be able to provide feedback representing a range of our members. The challenge of this proposal is that different stakeholders have different purposes for using proprietary ingredients (PI), and therefore the potential impacts will be varied and often opposing. PI suppliers, ingredient brokers, contract manufacturers, product sponsors and the TGA, all have differing views on how the proprietary ingredients system works for them and can work against them. While some parts of industry are under the misconception that they need to obtain a PI in order to make claims about an ingredient, this is only a small portion of the industry, and is not representative of the whole market.

From the information that has been provided it is not clear what the proposal is expected to achieve. While this proposal will 'clean up' a selection of PIs, it has not been communicated why these PIs represent a particular issue, and what value it will add to the system overall to remove these. In contrast, there are a number of concerns that industry has raised about the use of PIs that have not been addressed in any clear way by the proposal.

- Lifecycle management:
  While the proposal appears to be in relation to improving integrity of data held in TGA systems, the proposed amendments to the PI framework do not address ongoing issues around data integrity and lifecycle management. There are a number of challenges involved in the ongoing management of, and making necessary changes to, existing PIs. The current proposal does not appear to address these concerns. CHP Australia had been hoping to see a broader project initiated in this area associated with the digital transformation project. Given that PIs have many practical functions when used appropriately it is disappointing to see that the current project does not have the scope to improve lifecycle management of these ingredients and instead suggests removing a designated set of PIs without an explanation of how this provides a tangible benefit.

- Flavours, fragrances, and colours:
  There are ongoing issues with PI flavours, fragrances and colours and the need to include all components of these in the Permissible Ingredients Determination if these are to be used in listed medicines. It would be helpful if there were common expectations and reasonable cut off limits so that the TGA did not have to insist on a full assessment of every component of every PI no matter how low the concentration in the finished product. A review of the PI framework, particularly for flavours, fragrances, and colours, that allows for a reduction of regulatory burden and harmonisation with international requirements would provide a number of benefits to industry while streamlining the workload for the TGA.

- Intersection with the publication of PI information:
  Aside from PIs that are flavours, fragrances, and colours, ingredients in PIs are now published on the public ARTG summary. This creates an issue for sponsors as this information is not visible to them during the preparation of a new medicine application. This is a very real issue for sponsors as they may uncover ingredients in the public summary that they were not advised the product contained and may cause issues for the finished product presentation or consumer perception about the product. While the sponsor can ensure they are aware of any ingredients that need to be declared e.g. allergens, there may be ingredients used that the sponsor would prefer were not in their product, or they may have chosen differently if they were aware of the presence prior to submitting the application. The current proposal does not provide any mechanisms for addressing this issue, and CHP Australia would like to see further discussion and resolution of this concern.

Our primary concerns with the proposal as presented relate to:

- Transition
- Listing/labelling costs
- Possible GMP/licensing impacts
- Information availability/disclosure
- Risk of removing herbal active PIs
- Definitions of PI purpose
- Management of 26BB Determination issues

Transition

Members note a substantial amount of uncertainty about the intended transition arrangements. While the proposal suggests that existing products will continue to be able to use their existing PIs it is not clear how long this will endure for and how this is likely to work within the ARTG i.e. with ongoing validation of product changes. Members have suggested that it may be better to have formal transition arrangements that resolve some of the underlying data integrity issues and allow for PI numbers to be removed in a way that minimises impacts on ARTG entries and labelling.

Listing/labelling costs

CHP Australia is concerned about unintended costs and labelling changes that may occur as part of this transition approach. By avoiding a clear transition framework there is no transparent assessment of the costs that will be incurred due to this change. For example, for sponsors utilising 'excipient mixes' if they change their ARTG entry to include a different PI with a specific purpose this will not be able to be completed as a grouping application. This change will trigger a new ARTG number and subsequent label changes, even though they may be adding exactly the same ingredients to their product. Similarly, suppliers of PIs may elect to no longer supply a specific PI formulation and make changes to this formulation when they are obliged to submit a new PI type. The commercial arrangements underpinning the PI supply framework have a high potential to transfer costs onto sponsors that are not being considered as part of the proposal.

Possible GMP/licensing impacts

CHP Australia holds substantial concerns about the potential long-term impacts of this proposal on GMP licensing and clearance expectations. Sponsors who list products containing active premixes and active herbal extracts don't have to hold GMP clearances for these ingredients as there is no capacity to add an API as a step of manufacture to the listing application and this step is treated as part of the manufacture of the raw material. CHP Australia is concerned that the removal of active PIs, that neatly capture some of these manufacturing processes, will increase GMP obligations by making the ingredients and processes appear to be a step of blending in the finished product manufacture, which would require a finished product manufacturers license or certification. If the intent of this proposal is not to increase GMP obligations and costs for sponsors of listed medicines, then this should be clearly articulated, and necessary changes made to guidance materials to support the current expectations. Alternatively, if this proposal is intended to change the GMP status of these ingredient blends then this should form a transparent part of the consultation regarding the expected increase in regulatory burden and cost.

Information availability/disclosure

Sponsors report current difficulty in obtaining formulation information from PI suppliers – the removal of these PIs could improve this challenge by requiring the information to be shared, or it could lead to reformulation/relabelling to remove the PI where the supplier refuses to disclose information.

Requiring Sponsors to individually input the entire formulation of a PI into their listing application also presents an increased risk of listing errors. Multiple sponsors inputting a complex formulation multiple times is far more likely to result in errors than one supplier listing a PI formulation and providing a PI number for their customers to use. This effectively shifts the administrative burden from the PI supplier to the finished product sponsor, who needs to ensure proper traceability of lifecycle changes to the mixture, and needs to manage any changes to ingredients associated with the PI in their ARTG entry.

Changes to information within the ARTG related to PIs could also have impacts on export arrangements as this could be perceived by the importing country as a change to the formulation and invalidate an existing export certificate (CPP, CLP). The complex process involved in seeking approval for many export markets means that what is perceived as a simple process change for the TGA could introduce substantial costs and regulatory burden beyond the impact on ARTG and label changes in the Australian context.

There has not been a detailed and transparent consideration of the commercial or functional impacts of this proposal, and these will need to be considered in further consultation.

Risks of removing active PIs

Active premixes and active herbal extracts can have quite complex processing steps, requiring this information to be entered individually into the ARTG by each product(?) sponsor introduces the risk of multiple errors. Given that the experience levels and technical expertise of sponsors can be quite varied, this increases the risk of listing errors when complex processing steps need to be distilled into a form that can be entered into the listing portal. The advantage of having these ingredients established as PIs is that the supplier, who understands the ingredient, can enter this information once into the PI application.

CHP Australia members also raised concerns that the removal of PIs for active pre-mixes may be a disincentive for investment in clinical studies due to a lack of intellectual property protection. In effect the proposal requires provision of a

greater amount of potentially commercially sensitive information while removing the market protection benefits of an active premix.

Definitions of PI purpose

CHP Australia notes the proposal to remove "excipient mixes" in favour of applicants who want to continue using PIs to include these under a category description that is more meaningful. In addition to the previous points raised about the potential for this to incur regulatory costs and impacts, we request further consideration of why so many PIs were listed under the more general description of 'excipient mixes' and whether this relates to a lack of utility of the definitions provided. It may be that there is a need for new specific categories to be provided. From a quick scan of members' PIs, it looks like these could be captured in other categories, however CHP would like further information on the process to add additional categories and consideration of providing clearer definitions for the existing categories.

Management of 26BB Determination issues

During the development of the 26BB database there was a project undertaken to ensure that all ingredients currently used in all PIs were added to the 26BB Determination where possible. Members have noted some concerns that expanding a range of PIs may reveal some oversights from this project or some other inconsistencies. Given the proposed transition is not a time limited or structured process this makes it very difficult to systematically deal with any inconsistencies or needs for correction to the 26BB Determination that may arise. CHP Australia would like to see a clearer discussion of how any inconsistencies can be addressed in a way that minimises regulatory and cost impacts from this proposal.

Conclusion

This proposal is presented as a simple administrative change; however, CHP Australia holds a number of concerns about potential for unintended regulatory and cost impacts. CHP Australia would prefer to see a comprehensive review of the PI framework, with potential for a more user-friendly database that allows for lifecycle management and provides an avenue for simplifying the listing of flavour, fragrance, and colour PIs. We recognise that this would be a much more substantial project with associated costs, IT development and likely legislative changes, however a more detailed consideration and consultation on the issues would be preferable, given that this proposal is still likely to present substantial regulatory challenges and costs to industry for minimal benefit.