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Updates to Australian medicine labelling rules to support medicine safety

- Listed Medicine Large Oral Dosage Forms

CMA Submission: - Part 3: *Improving information on listed medicines about large solid oral dosage forms intended to be swallowed whole*

CMA appreciates the opportunity to provide feedback on Part 3 of the consultation on updates to Australian medicine labelling rules to support medicine safety - *Improving information on listed medicines about large solid oral dosage forms intended to be swallowed whole*.

Complementary Medicines Australia (CMA) is the peak body of the complementary medicines sector, representing approximately 80% of the sector by sales of complementary medicines. Australia is the source of the highest quality manufacturing environment in the world for finished product vitamins, minerals, and herbal preparations. Our members include stakeholders across the value chain, including manufacturers, raw material suppliers, distributors, consultants, retailers, and allied health professionals. CMA supports high quality and safe use of medicines through appropriately balanced and pragmatic risk-based regulation.

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Part 3

Question 12

Do you agree that the proposed dosage unit size thresholds for the labelling requirements are set at the right size? Please explain your answer. If you do not think the proposed size thresholds are set at the right size, do you think they should be smaller or larger than what we have proposed? Please ensure you read Appendix F and provide evidence to support your proposal.

The proposed dosage unit size thresholds for introducing a range of new labelling requirements apply to:

Tablets where:

- the length or largest dimension is greater than 22mm, or
- the width, widest dimension or diameter is greater than 9mm
    - including round tablets with a diameter greater than 9mm.

Capsules where:

- the length or largest dimension is greater than 23.3mm, or
- the width, widest dimension or diameter is greater than 9mm.

The Regulator Performance Guide requires that proposals are risk based and data driven[1]. This principle describes that regulators manage risks proportionately and maintain essential safeguards, while minimising regulatory burden, and are to leverage data and digital technology to support those they regulate to comply and grow.

Regulators, including the TGA, do not seek to avoid all risks - that would be impossible - but its risk management approach is about reducing the impact of risk to an acceptable level in a way that minimises regulatory burden. CMA is firmly of the view that the consultation proposals do not achieve this. The analysis of a much broader dataset is required to identify the dimensions associated with risk and inform the action required. We have conducted a member survey and determined that the proposed size dimensions would on average capture 35% of Listed medicines. This is significantly out of proportion to the adverse event (AE) risk for the majority of these products. This is demonstrated in this submission through the data we have been able

[1] https://www.finance.gov.au/government/managing-commonwealth-resources/regulator-performance-rmg-128/principle-2-risk-based-and-data-driven

to gather within the short consultation timeframe. There are *no to negligible* numbers of reactions to most products captured by proposed dimensions when compared AE data.

CMA recognise the importance of drawing on literature reporting on dimensions associated with swallowing difficulties, but limitations with these sources should also be acknowledged. For example, Punzalan et al. (2019) concerned AEs reported between to the US FDA CAERS between 2006 and 2015, while the German survey was conducted in 2010-2011 (Schiele et al., 2013). Not only are these studies based on data a decade or more old, but it is likely that a smaller proportion of the medicines of that era were coated tablets and soft gels compared to contemporary Aust L products, especially for larger dosage forms.

Based on available data and information supplied by either the TGA Database of Adverse Event Notifications (DAEN) and/or sponsors, at the *far end* of the dosage form size spectrum, there is some increased frequency of data on increased level of risk, particularly to older adults. This has been driven by data on very large dosage forms such as 2000mg fish oil, some of which have been phased out, as discussed later in this submission.

Adverse events to all registered medicines (excluding clozapine), and OTC Registered medicines as a subset, are now outstripping the number of AEs to Listed medicines and have size dimensions that exceed this proposal by more than 35% in addition to sales volumes that dwarf the top ten selling Listed medicines. This creates a major labelling difference between a large number of self-selected medicines side by side in supermarkets and pharmacies when medicines not labelled with the requirements are *significantly* larger than medicines labelled with the requirement, is not only confusing, but creating a new safety risk.

This data demonstrates that the current proposed size dimensions on most products are not justified, and that a more comprehensive Government dataset is required to implement changes on most of the currently captured products, excluding a handful of the *very large* dosage forms that have some data available.

Problems identified with these size dimension proposals are outlined in detail below.

Problem 1. Inappropriate data and Insufficient data analysis.

Validity of dataset

The validity of the dataset used to justify the need for warning statements on Listed medicines alone is questionable, since the criteria employed introduces bias. The data retrieved from DAEN and used to inform the public consultation was selected using a range of appropriate reaction terms, but then narrowed to exclude medicines where the name was not specified. Given that it is the characteristics of the dosage form that is being investigated as a primary risk factor for choking, it is hard to understand the justification for excluding reports based on the lack of the name of the medicine. Reporting an AE requires time and commitment from a consumer, health professional or sponsor and it is inexplicable that these reports were considered out of scope of this investigation.

Many of the excluded reports concern medicines like OTC paracetamol that are intended to be self-selected in supermarkets and pharmacies just as Listed medicines are. As illustrated below, this has led to significantly biased results creating unjustifiable policy proposals.

Other concerns with the data analysis used to inform the public consultation include the failure to consider the incidents from a longitudinal perspective and the lack of a detailed breakdown of the characteristics of the medications involved. The TGA, with its access to ARTG entries for Registered and Listed medicines is therefore in a position to provide more insight into how characteristics of oral dosage forms correlate with choking-type AEs.

Clarity and transparency of reported consultation figures

CMA is aware that in some cases, not all information on AEs is provided to the TGA and only a subset of the information available in AE reports may be made available to the public via the DAEN.. Therefore, it is difficult for external stakeholders to reproduce an exact comparison of the data used in the consultation paper.

To better understand the AE figures for Listed medicine provided in the consultation, a search of the DAEN using the same inclusion criteria was conducted.

Which numbers are correct?

The consultation paper states that if cases related to clozapine are excluded, 94% of cases (287/306) relate to Listed medicines; *i.e.* that 19 reports for Registered medicines are included.

However, using the same criteria stated in the consultation paper[2], a search of the DAEN in May 2024 provided a total of 296 medicines; 271 Listed medicines and 25 Registered medicines.

While we cannot determine exactly why there is a difference, it is possible that the consultation figures included an additional 6 medicines that are not intended to be swallowed whole (chewable) for listed medicines; one vitamin D medicine that is a Registered medicine; or 5 Registered medicines in the count for Listed medicines, because they are a multivitamin/mineral preparation.

The consultation paper[3] also states the number of choking related AEs reported to the TGA for Registered complementary or OTC medicines is very low, **1.5%** [5/326]. The footnote reference for this information refers to the same criteria used to conclude that **94%** cases (287/306) involved Listed medicines. However, it is also stated using the same footnote[4] that analysis of Australian reported AEs shows that of the 326 reports related to medicines with 4 or more choking-related reports each, **88%** (288/326) involved Listed medicines. The difference in analysis using the same data and reference is impossible to understand. The latter number assumes that there are AE reports for 38 Registered medicines, which equates to **12%** [38/326].

Introduction of bias

The selection of inclusion criteria for reported AEs in DAEN can significantly influence the results. Our review of the DAEN[5] used the same criteria as the TGA criteria with 2 exceptions:

a) the inclusion of only 4 or more reports for a medicine and

b) the exclusion of medicine where no trade name was provided.

Including sole suspected medicines and reports associated with medicines that lacked a trade name revealed entirely different results. A total of 641 medicines were identified. If reports for clozapine [21] are excluded per the TGA's rationale, a total of 620 medicines are included, approximately:

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[2] Data to 19 February 2024. Reaction terms: choking, choking sensation, foreign body in throat, product size issue. Sole suspected medicines only. Medicines were excluded if they were not solid oral dosage forms intended to be swallowed whole, or if the medicine name was not specified and could relate to dosage forms that are not solid or oral. Medicine names with 4 or more reports each were then selected. 20 Clozapine containing medicines excluded.

[3] p42

[4] p40

[5] Included: reports to 19 Feb 2024; sole suspected medicine; reaction terms Choking, Choking sensation, Foreign body in throat, or Product size issue; products intended to be swallowed whole; medicines with no trade name. Excluded: 1 report for 'Slippery Elm' [usually in powdered form] and 1 report for 'Ferrous Sulphate' [not specified whether RM or LM]

- **65%** (400) Listed medicines;
- **35%** (220) Registered medicines.

This indicates an over inflation of the consultation's stated 94% of reported cases for listed medicines by approximately 35%. This is a significant discrepancy, misleadingly implying that Listed medicines are associated with a third more choking events than OTC medications than a more complete data set shows.

Concerningly, at least 42 paracetamol reports were excluded from the TGA's criteria, compared to 9 included, because no trade name was provided. However, from our limited sampling exercise, we found that at least 17 paracetamol medicines exceed the proposed consultation thresholds, of which 9 exceed the proposed >9.0mm for width/diameter by ≥38%, median 42%.

In the last 6 months there have been more reports for paracetamol alone than for all listed medicines, indicating a clear signal for paracetamol that cannot be dismissed, even in the absence of a trade name, if the intended goal is consumer transparency to help protect them from swallowing risks.

While the decision to include data about medicines with 4 or more choking-related reports may have been made in good faith, as a more reliable signal, logic suggests that a focus on the characteristics of each medicine or medicine type that cause a choking is warranted, as each report informs this question.

The lack of reliable, complete and convincing datasets undermines the validity of the proposed consultation's threshold. Consider Table 5 of the consultation paper[6] which is populated with numbers drawn from DAEN reports associated with Aust L medicines only, rather than from all self-selected medicines. This decision unnecessarily restricts the sample size, reducing the reliability of the information (note too that the search terms employed here are not identical to those quoted earlier in the public consultation document).

Many stakeholders reading this submission have neither the time or the training to take on board the details of the footnotes, independently check the data or understand the implications of the various decisions in the data selection. The expectation of a public consultation paper is a document that is transparent and provides clear, unbiased information upon which robust and informed policy development can be based. This consultation paper has not met that standard. Stakeholder responses to a consultation based upon incorrect or biased data and analyses cannot be relied upon.

[6] p43

A significant change in data since 2020 has not been taken into consideration

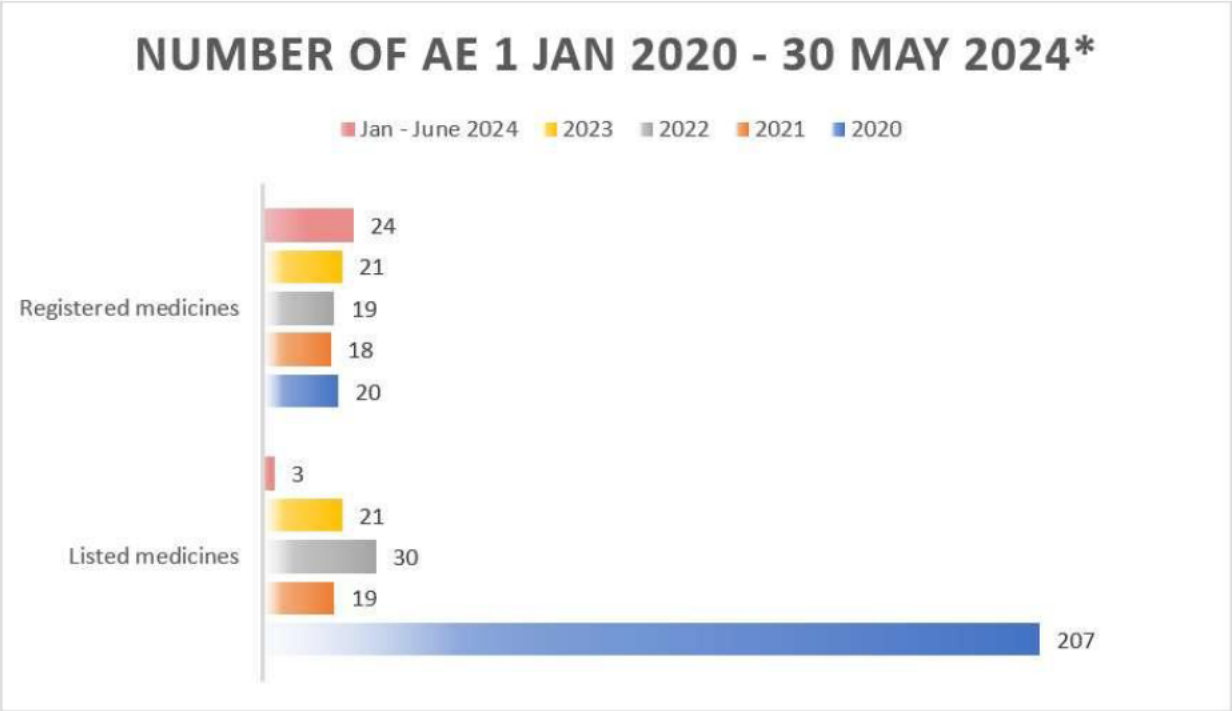
An assessment of the data received by members against the reported choking related AEs to February 2024 revealed that at least 197 of the reactions reported for listed medicines were attributed to 31 medicines that are no longer on the ARTG, and that the number of choking related reactions associated with Listed medicines has dropped significantly since 2020. This demonstrates industry's commitment to safety through implementing measures such as product reformulation where clear and important signals are identified.

For example, CMA has received sponsor information that the reformulation of tablets to reduce length, following a number of AEs, resulted in a significant reduction of choking related adverse event reports for those products (zero adverse events in 3 years), despite them being taken by the same population. Similarly, reformulation to include film-coating on a medicine that previously received AE reports has resulted in zero AE reports since reformulation.

Sponsor-based pharmacovigilance has detected safety signals associated with one-a-day dosage units and many of these have been phased out to mitigate risk to consumers in spite of consumer preferences and thus market-driven demand for them. This is confirmed by the longitudinal analysis of selected DAEN data illustrated below.

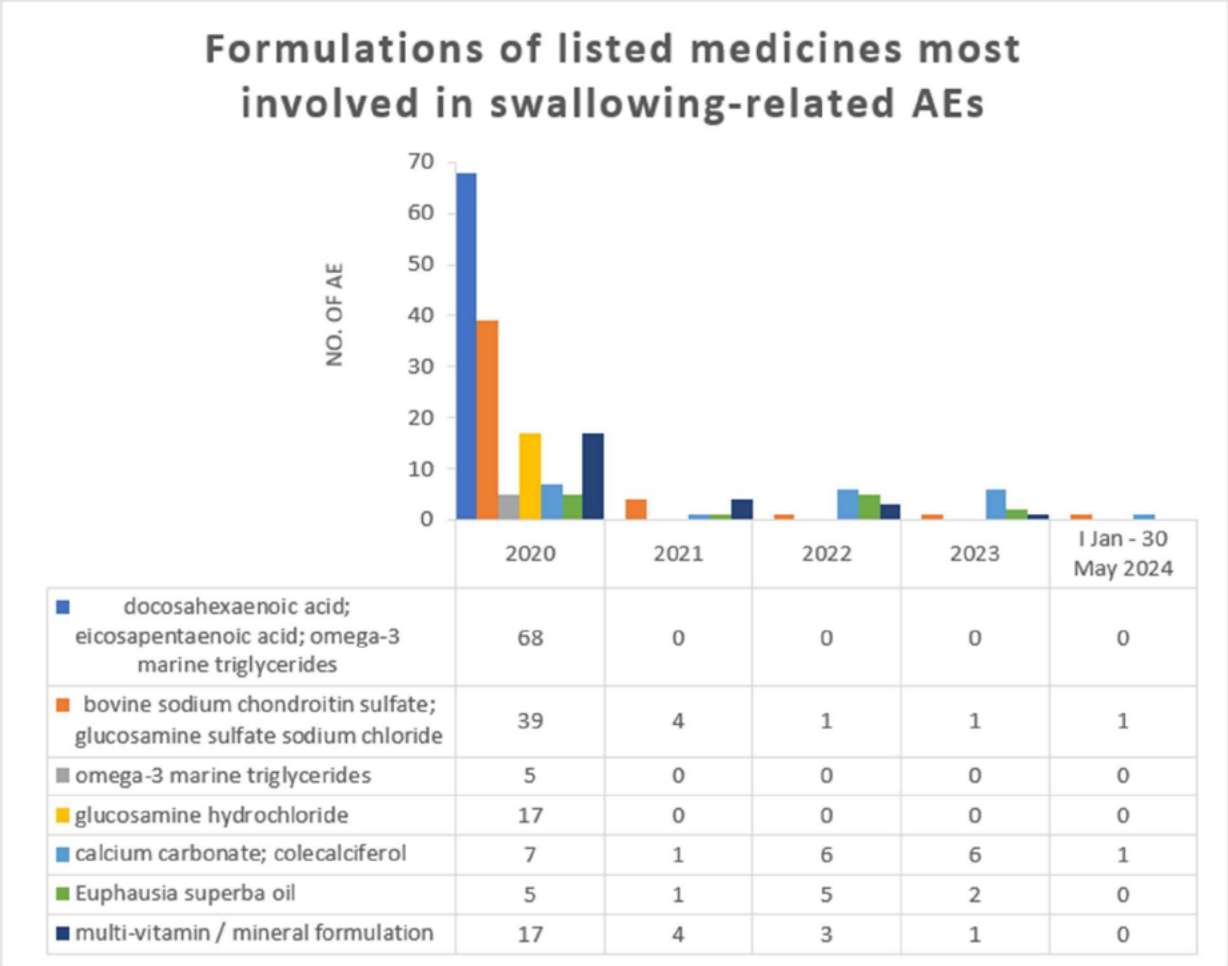
Notably, AE reports for sole suspected listed medicines generally have reduced by >98% since 2020, compared to a 4.8% increase in Registered medicines in the same period

Figure 1. Comparing Listed & Registered Medicines Adverse Events 1 Jan 2020 – 30 May 2024.



* DAEN search: Sole suspected medicine excluding Clozapine; only medicines intended to be swallowed whole; Reaction Terms Choking, Choking sensation, Foreign body in throat, or Product size issue; those with no trade name included.

Figure 2. Formulations of Listed medicines most involved in swallowing -related cases 1 Jan 2020 – 30 May 2024.



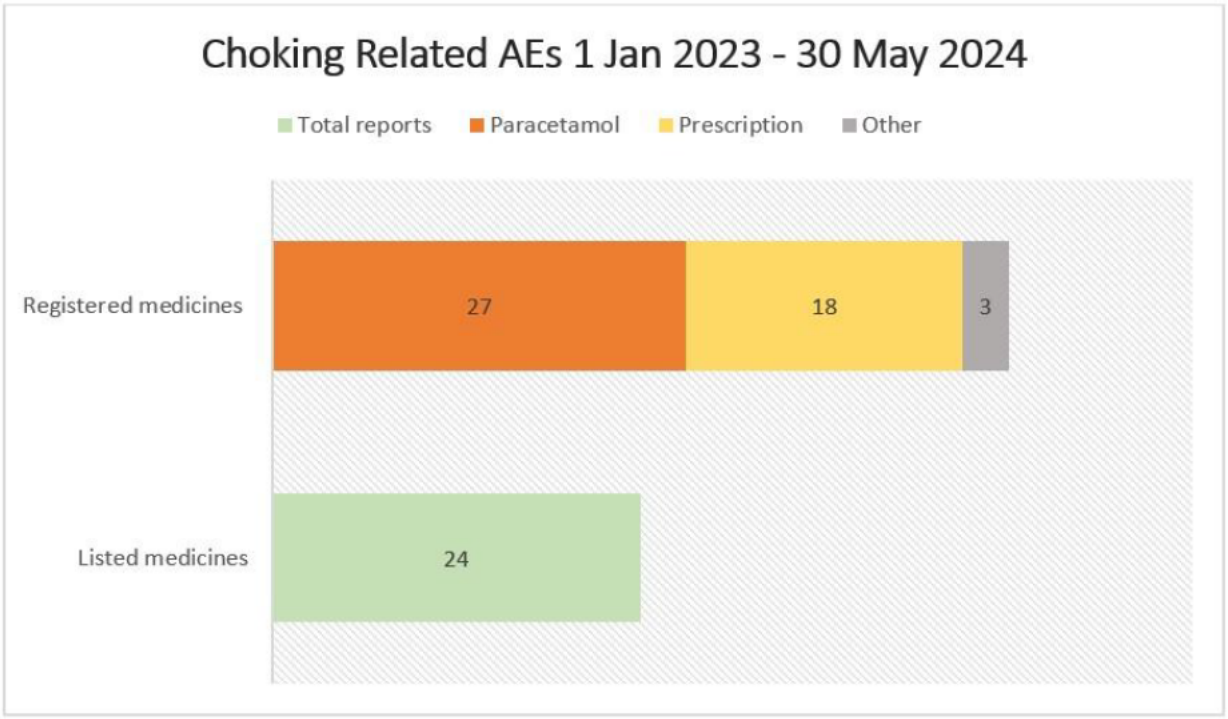
	2020	2021	2022	2023	I Jan - 30 May 2024
docosahexaenoic acid; eicosapentaenoic acid; omega-3 marine triglycerides	68	0	0	0	0
bovine sodium chondroitin sulfate; glucosamine sulfate sodium chloride	39	4	1	1	1
omega-3 marine triglycerides	5	0	0	0	0
glucosamine hydrochloride	17	0	0	0	0
calcium carbonate; colecalciferol	7	1	6	6	1
Euphausia superba oil	5	1	5	2	0
multi-vitamin / mineral formulation	17	4	3	1	0

* DAEN search: Sole suspected medicine; only medicines intended to be swallowed whole; Reaction Terms Choking, Choking sensation, Foreign body in throat, or Product size issue; those with no trade name included.

The necessity of using accurate data for policy development is demonstrated in this analysis of reports in the DAEN between January 2023 to the end of May 2024. The reaction terms provided in the TGA consultation paper (Choking, Choking sensation, Foreign body in throat, or Product size issue) were employed, but not all the exclusions (see foot note to figure above). The search revealed there were **twice as many AEs** attributed to registered medicines than listed medicines – this included *all* medicines intended to be swallowed whole, not only those included in the TGA criteria.

Of the 95 reports during this time, and excluding clozapine and dosage forms that are clearly not oral, such as vaccines, liquids and inhalants, 72 reports remained. **48 reports related to registered medicines**; and **24 reports related to listed medicines**, one of which was not on the ARTG. Drawing conclusions from the data selected and reported upon in statements made in the public consultation erroneously suggests that listed medicines are currently the most important contributor to medicine related choking risk.

Figure 3. Choking related AEs for Sole-suspected Medicines intended to be swallowed whole, 1 Jan 2023 – 30 May 2024



* DAEN search: Sole suspected medicine excluding Clozapine; only medicines intended to be swallowed whole; Reaction Terms Choking, Choking sensation, Foreign body in throat, or Product size issue; those with no trade name included.

Problem 2: Listed and Registered – is a discrepancy in labelling policy justified?

The consultation paper acknowledges the most consistently identified risk factor is the larger size of some dosage units[7] and that the risk applies to **all large solid oral dosage forms** that are intended to be swallowed whole[8]. Despite this, it does not capture dosage forms from both classifications (Listed and Registered) that are associated with the potential for harm from swallowing due to their size.

Much of the available literature on dosage form size and choking incidence relates to medications that are taken under the supervision of a general practitioner, or in a pharmacy or healthcare setting (Schiele et al., 2013; Lau et al., 2015; Fields et al., 2015; Overgaard et al., 2001; Marquis et al., 2013; Kabeya et al., 2020; Notenboom et al., 2017), demonstrating the issue is not one limited to listed medicines. As discussed in Problem 1 above, the more complete data shows a breakdown of 65% reactions to Listed medicines (mostly from 2020 which reduced significantly after product discontinuations) and 35% for Registered medicines.

Appendix F of the public consultation paper argues that registered medicines, which are assessed for efficacy, may be associated with a slightly higher risk to patients since their benefits have been pre-assessed. This is a spurious argument, particularly for self-selected OTC medicines that have a wide variety of alternative brand options available, since any choking risk posed by the size of an oral dosage form is entirely independent of the medicine it delivers.

Listed medicines are prevented by the *Therapeutic Goods Act 1989* from having their benefits pre-assessed if the claims used do not meet higher-risk criteria. Further, there are several permissible indications on these medicines that have been pre-assessed for their benefits therefore, this is an unfair value judgement.

The Listed medicine system enables the availability of a wide range of low-cost to consumers, including for medicines in large dosage forms that are frequently recommended by medical practitioners, including multivitamins, calcium, omega 3/fish oils, etc.

[7] p48
[8] p25

Safety risk through misleading labelling of comparable products

If the proposed dimensions were applied equally, both Registered and Listed medicines would be affected, including high volume self-selected medicines, particularly paracetamol, ibuprofen and aspirin.

Of the 52 registered medicine reports illustrated in Figure 3, 18 related to prescription medicines, while 27 were associated with the paracetamol tablets alone. In the same period of time 24 AEs were recorded from *all* listed medicines.

A very limited sample of 48 Registered OTC medicines available for self-selection in pharmacy and supermarkets that are intended to be swallowed whole, were purchased and measured against the proposed limits requiring labelling changes for listed medicines.

From a limited sampling exercise, it is evident that there are at least:

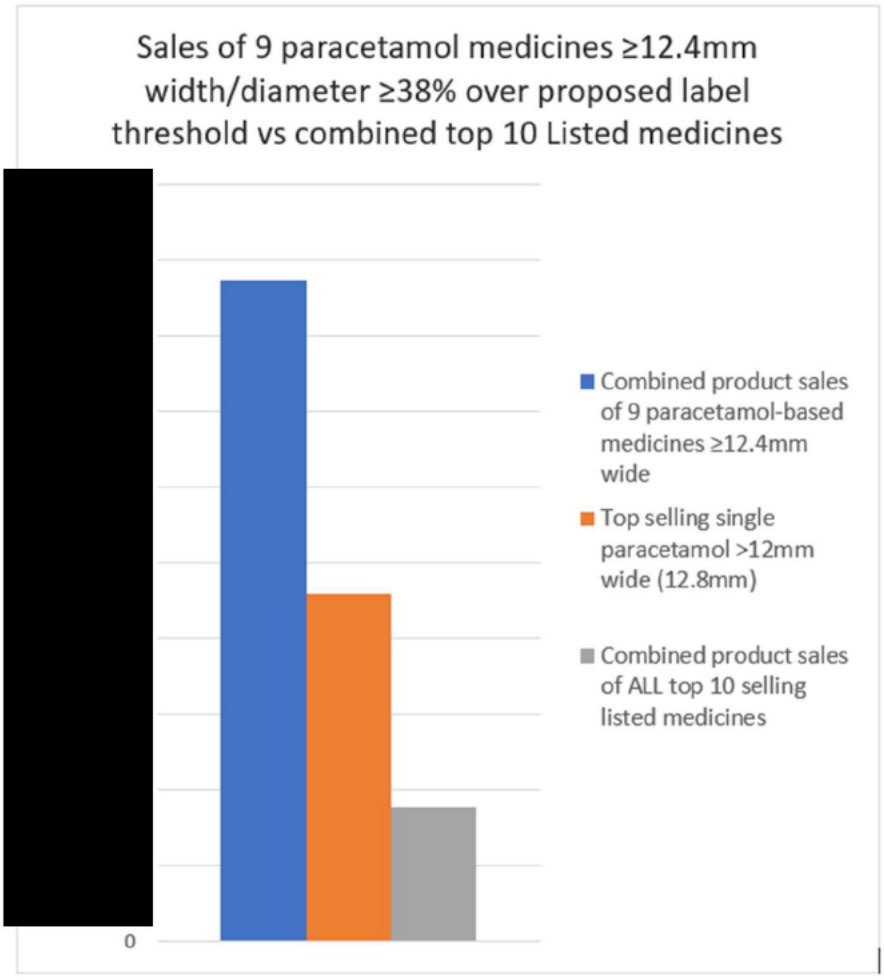
- **31** commonly self-selected OTC medicines that exceed the dimensions in the proposal[9]
    - **2** of which are indicated in children age 2+ whose directions for use include swallowing whole
- **17** paracetamol self-selected medicines that exceed the dimensions in the proposal
- **11** OTC medicines that equal or exceed 12mm width/diameter
- **9** paracetamol-based medicines that exceed the proposed >9.0mm for width/diameter (12.7-12.9mm, median 12.8mm) by **≥38%**, median **42%**.

As the proposal currently stands, any round tablet that is a Listed medicine with a diameter of **9.1mm** or greater would require 'Warning: Large Tablet' and 'actual size' with a true-to-size image. However, 9 Registered OTC medicines tablets would not, despite a diameter between **12.4** - **12.9mm** that exceeds the proposed threshold by ≥38%.

The combined annual sales volume of just 9 of these medicines for the last 12 months exceeds that of all top-ten selling Listed medicines combined, by a factor of 5 (Figure 4). It is unjustifiable that this obvious lack of disparity in labelling is due to a classification that makes no difference to a consumer's ability to safely swallow a tablet.

[9] Refer Appendix A

Figure 4[10]. Nine paracetamol products that exceed the proposed dimensions by ≥ 38% and outsell the combined top 10 listed medicines by sales by a factor of 5.



The effect of continuing with a difference in labelling policy despite some common OTC Registered medicines being well above the proposed thresholds and the enormous difference in sales volumes between OTC and Listed medicines, is illustrated below.

[10] Refer Appendix B

Actual Size of 9.1mm and 12.8mm tablets, when viewed at 100% or printed on A4

Listed Medicine self-selected:

9.1mm diameter

> Requires:

- Image of actual size
- 'Actual Size'
- 'Warning: Large Tablet'

Registered Medicine self-selected:

12.8mm diameter[11] (median exceeding 12mm):

> No requirement or warning.

Size comparison of 9.1mm to 12.8mm:

The general public are largely unaware of the difference between Listed and Registered medicines. The difference in regulatory requirements for listed and registered products prompted the consumer advocacy group CHOICE to find out how much consumers understood. Information gathered from a national survey revealed that of 1052 people 80% had never actually noticed AUST L and AUST R numbers on the label of the medicine (Bray, 2018). Among the 142 people who were aware that the label contained these codes, many were not sure what the difference was between AUST L and AUST R medicines (Bray, 2018).

Most of the 29 products found were large round tablets, many of which have very large sales across the community, including older age-groups. This is important since as noted in the consultation, dysphagia is more prevalent among older adults (page 41). This problem appears to be exacerbated not only by size, but also by shape with round tablets being harder to swallow compared to capsules or oval tablets (Hey *et al.* 1982) .

[11] [redacted]

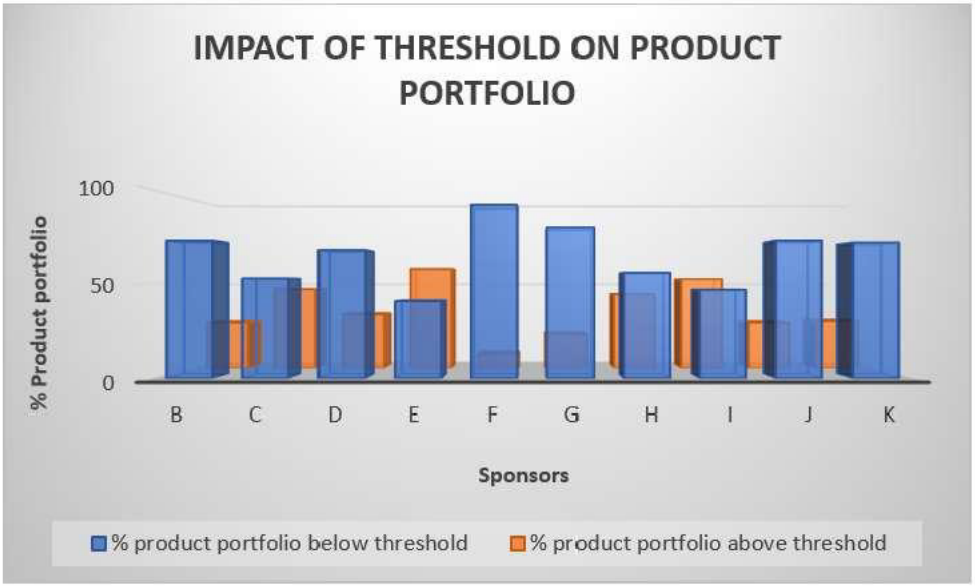
Since most consumers are unaware that Aust L and Aust R medicines are distinct categories, it is even less likely that they will be aware of any difference in labelling regulation. Thus, they may naturally assume the OTC medicines without warnings that are side-by-side on shelves with listed medicines carrying these warnings, are smaller and safer to consume, when this will often not be the case. This inconsistent approach lacks common sense and makes for poor and unsafe policy. The impact of dimensions, particularly width/diameter requires more study considering this new information.

There is an additional complication of many OTC products showing inaccurately sized images of dosage forms, which is further discussed in Problem 6, Item 3.a).

Problem 3: A broader review of Australian data does not support the proposed thresholds that capture an excessive percentage or proportion of products.

At the *far end* of the spectrum of tablet and capsule dimensions, our sponsor members acknowledge there are signals of greater difficulty swallowing for some individuals and they are willing to address this, *provided* that the policy is relevant and justified by the signals observed. However, the current proposal capturing approximately 35% of all products (ranging from 8 – 59% from 10 sponsor members), a level of change which is significantly out of proportion to member and TGA AE data. This significantly and unnecessarily increases costs for manufacturers, businesses, and consumers, as well as creating ongoing label impacts that for most products are not justified by the available data as discussed further in this part. It is important that further decisions about changes to regulation that will require complex logistical and financial investment from sponsors, are appropriate to the current risk environment.

Figure 5: Percentage of ten sponsors' product portfolio impacted by the proposed threshold dimensions[12]



The application of this information to a large proportion of products, rather than reserving it for the largest of dosage forms with more clearly defined signals and frequency, is likely to have the effect of conveying a less targeted and impactful message for genuinely larger sizes where the message is of greatest importance.

Appropriately limiting the impact to a defined smaller group of medicines has the advantage of being more closely correlated with the risk, reducing the problems associated with consumer desensitisation to frequently encountered warnings. This is discussed in Problem 6, Item 2.

Soft gelatin capsules

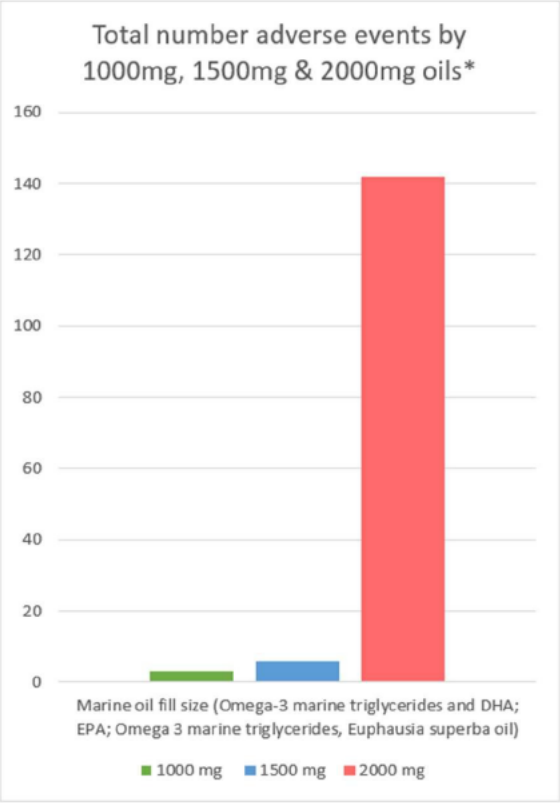
The consultation proposal provides a threshold for soft capsules of 23.3mm to align with standard hard capsule size 00 however, this proposal captures a significant proportion of all soft gel capsules, including those that cause no or negligible reactions. Specific data for soft gel capsules is not provided in the consultation, except that more AE reports were for soft capsules than other dosage forms. It also states that no convincing evidence has been provided to support that soft capsules should be subject to larger size thresholds. However, it is known to

[12] Refer Appendix C

industry that the DAEN reports including the underlying data relate of adverse reactions have been associated with only the very large dosage forms, and primarily, the 2000mg omega oils. Despite this, the proposed thresholds of 23.3mm long and 9 mm wide are to affect the billions of 'standard' capsules equivalent to a 1000mg size sold that are negligibly associated with AEs. The consultation refers to AEs associated with large soft gel capsules of fish/krill oil /omega-3 medicines[13] however, sponsors report a reduction in AEs due to discontinuation or reformulation, and this is reflected in recent DAEN reports (see Figures 2 and 3).

Given the limited timeframe with which to gather member information and AE data, marine/omega oils were also the only softgel category that could be practically reviewed. Adverse events and the available frequency were examined.

Figure 6. Adverse events for 1000mg; 15000mg; 2000mg marine oils currently on ARTG that are all over the proposed size thresholds for capsules

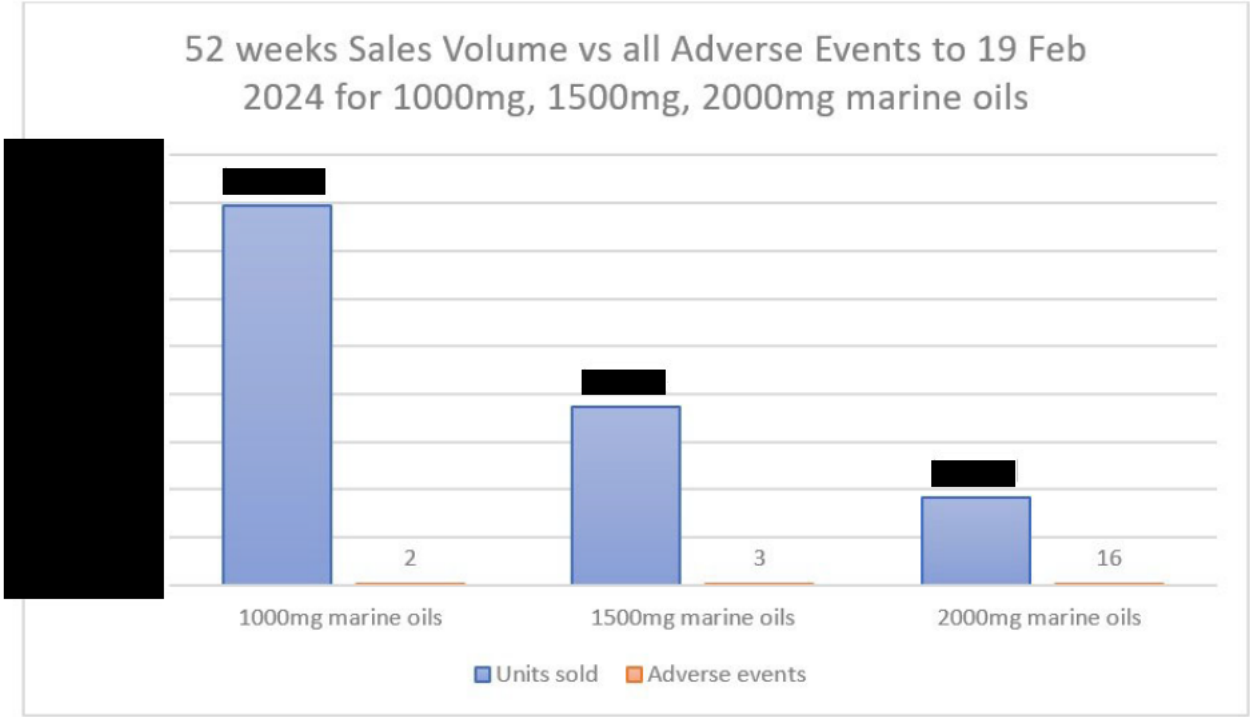


*Based on products with serious and non-serious AEs [DAEN data + (Sponsor data from 3 sponsors of 2000mg fish oil – minus any duplications from DAEN data)]where the quantity of active ingredient oil in the product was able to be identified[14].

Figure 6 includes both current products and products that have already been cancelled due to AEs received.

[13] p46
[14] Refer Appendix D

Figure 7. Frequency of adverse events to marine oil soft gel capsules currently captured by the proposed size thresholds[15].



*IQVIA Scan Total Pharmacy and Grocery (Coles and Woolworths), Unit Sales for 52wks ending 15 June 2024. Total AEs for current ARTG entries calculated using DAEN data to 19 Feb 2024 where product is known; and sponsor data, where provided to CMA. 'Marine oils' includes docosahexaenoic acid; eicosapentaenoic acid; omega-3 marine triglycerides; Euphausia superba oil.

Based on these omega oil figures, there is a:

- **1 in a million chance** of a choking related adverse reaction to a 1000mg capsule
- **4 in a million** chance of a choking related adverse reaction to a 1500mg capsule
- **43 in a million chance** of a choking related adverse reaction to a 2000mg capsule.

A 1 in a million chance of experiencing a choking related adverse reaction is an insufficient a risk to implement mandatory label regulations to a significant number of products. This is evidence that 1000mg soft gels roughly equivalent to over 26mm L and over 11mm W are excluded from this consultation. Please NOTE that one of the two AEs to a 1000mg oil was the only capsule over 26mm long, at 26.6mm long.

[15] Refer Appendix E

In addition to the above, some CMA members have provided information on the sizes of tablets and capsules that exceed the proposed thresholds, but have had nil AEs or complaints[16].

Below are figures of the exact sizes of a variety of soft gel capsules obtained from members:

Table 1 – Sizes of 1000mg marine omega oils

CMA Member	Length	Width
Manufacturer 1	21.5	10.5
Manufacturer 1	25.2	9.3
Manufacturer 2	24.6	9.3
Manufacturer 3	25.4	9.2
Manufacturer 4	22.8	11.07
Sponsor A	25.5	9.7
Sponsor C	24.5	8.7
Sponsor H	26.6 (one of the two AEs)	9.5

Table 2 – Sizes of 1500mg marine omega oils

CMA Member	Length	Width
Sponsor C	**25.5**	**11.1**
Sponsor H	**27.4**	**9.9**

Table 3 – Sizes of 2000mg marine omega oils

CMA Member	Length	Width
Sponsor C	**26.9**	**12.6**
Sponsor H (discontinued)	**27.6**	**13.1**
Sponsor H (discontinued)	**31.9**	**11.5**

Size information for 1500mg and 2000mg is more limited but more information could be obtained.

[16] See Appendix K

Additional evidence supporting larger thresholds for soft gels, excluding very large forms

The literature supports the above data. Soft gel capsules have been demonstrated to improve swallowability (Gullapalli, 2010) because of their shape and flexible coating, and can be larger than tablets whilst not inhibiting swallowing (Kerins, 2020). The EMA Reflection paper (2020) also notes that soft capsules can be easier to swallow than hard capsules for older adults.

The consultation notes that Kerins (2020) indicates that soft gels were the second highest dosage form precipitating AEs after tablets (coated and uncoated) however, the percentage of AEs for soft gels was much lower than for tablets: Tablets are presented as accounting for approximately 86% of events. Additionally, Kerins' summary (2020) on known tablet and pill parameters affecting deglutition provides that tablets and (hard) gelatin capsules are worse than soft gelatin capsules.

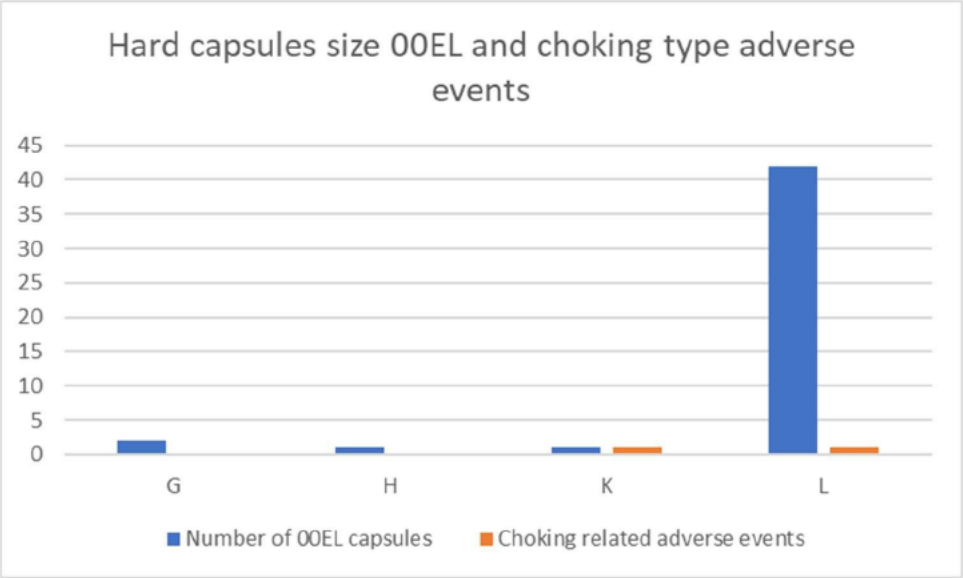
The consultation also refers to Kerins (2020), commenting that 31% consumers preferred tablets/caplets; 19% preferred capsules; while only 11% preferred soft gels. However, there are other studies and market research to suggest consumer preference for soft gel dosage forms. For example, a survey on consumer perception of soft gels in comparison to other dosage forms found that ease of swallowing was one of the drivers for consumer preference for soft gels: oval soft gels were more frequently identified as easy to swallow than any other dosage form, followed by gelatin-coated round tablets (Jones & Francis, 2000). New coating technologies may account for the difference in the findings.

While there is not a great deal of literature available, that which is available is supportive of the earlier findings that larger thresholds for soft gels are justifiable.

Hard capsules

Four sponsors provided information regarding their use of size 00EL hard capsules. This covered a total of 46 products. Just two choking-type AEs were recorded[17].

Figure 8. Adverse events in hard capsules size 00EL



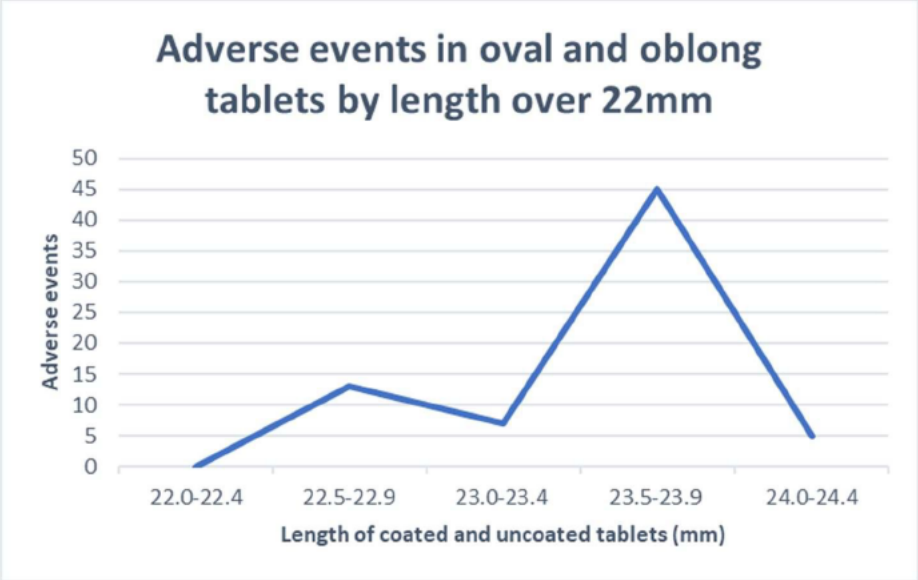
Based on this data, regulatory action at 00EL is not warranted in the immediate term, but further monitoring and assessment for consideration during the Sep 2026 TGO is likely warranted.

[17] Refer Appendix F

Oval/Oblong Tablets

Detailed information about the dose forms associated with AEs was provided by three sponsors. This reveals that the number of AEs rises sharply at **23mm L** and **11mm W** in oblong and oval tablets[18].

Figure 9. Adverse events in oval and oblong tables by length

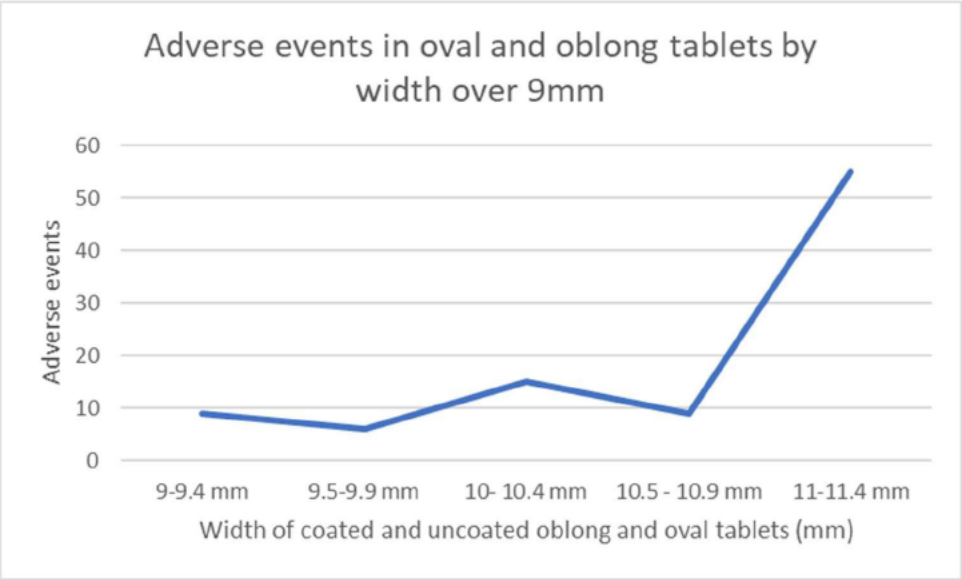


Adverse events associated with 21 products measuring over 22 mm are captured in Figure 7 above. Each of these tablets were *also* over the threshold width of 9mm wide, indicating the importance of length plus width together as a predictor of outcomes rather than length or width alone. A larger sample size is preferable; however, this was the maximum sample size we were able to obtain in the consultation period.

A further six tablets, less than 22mm in length, that exceeded 9mm in width were associated with choking-type reactions, and are included in Figure 8[19], bringing the number of the products in the Figure 8 up to 27.

[18] Refer Appendix G
[19] Refer Appendix H

Figure 10. Adverse events in oval and oblong tablets by width over 9mm



Limitations with data available to CMA

Three major sponsors provided information about each product in their portfolio over the threshold dimension with details of the dosage forms and AEs. However, many small and medium sized sponsors simply do not have the resources or capacity to provide any, let alone all, relevant details to us particularly in a short timeframe. CMA and/or TGA could work harmoniously as relevant parties to gather more information where required.

Conclusions for Oval/Oblong Tablets

Despite the limitations, this sample nonetheless captures the dimensions of 27 dosage forms associated with complaints and choking-type reactions and establishes a correlation to the length and width at which the risk of AEs increases, that exceed the proposed thresholds.

The consultation paper has not stratified dimensions above 22mm and 9mm, but only provided a total figure. The new industry data provided in this paper, indicating there is a negligible frequency of reactions between 22-23 mm long and 9-11mm wide, together with the lack of reactions between 2021-2024, brings into question the validity of regulatory action at the current thresholds impacting a significant proportion of products.

Without further datasets, with a frequency rate strongly justifying action is necessary, the currently data-driven size thresholds apply to oval/oblong tablets above 23.0mm long and above 11.0mm wide.

Resolving Problems of Size Thresholds, Data, & Regulatory Impact

Problems with the consultation data, combined with changes to sizes, labels and coatings that sponsors have already made demonstrating significant improvement since 2020, and the clear trends demonstrated by the new datasets drawn from CMA members, provides a conflicting view of the true risk associated with large solid oral dosage forms. CMA members and existing changes implemented by sponsors indicates a willingness by industry to tackle this safety issue if it is within appropriately data driven policy settings with achievable impact implications. Unfortunately, this is not what the public consultation is proposing.

Adverse events data captured in the next few years and followed up to ensure relevant characteristics are collected, including actual sizes that can be better stratified to frequency rates and risk profile, would provide further insights into how sponsors can act to improve their medicine safety and what specific policy settings are likely to be most influential in further reducing risk. This permits the confident development of effective, well-supported and world leading policy on Listed and Registered medicines that could be supported by stakeholders.

There are two options to proceed in the short term, which is using the still-limited but nonetheless convincing and only datasets that are available (Option 2 below), or conducting an even more comprehensive data review to verify with absolute surety that any policy decisions that are create impact (Option 1 below) are based on a fully supportable dataset.

These options acknowledge that:

- It should be examined more thoroughly whether film coatings and soft gels have an effect that reduces risk.
- The risk associated with many products reported to have caused AEs reactions has already been mitigated by product discontinuations, reformulations and/or labels updated under an existing Condition of Listing.
- Adverse event reports for Registered medicines are currently on par with Listed.
- OTC medicines that are larger, sometimes significantly larger, than those proposed for Listed medicines would provide consumers inaccurate and confusing safety information
- To inform a more complete risk assessment it would be ideal to obtain follow up reports of choking-related AEs seeking specific information on dimensions and characteristics of the dose form, together with information about the age or other characteristics of the person and whether liquid was taken while swallowing.

Consultation Summary Response on Size Thresholds

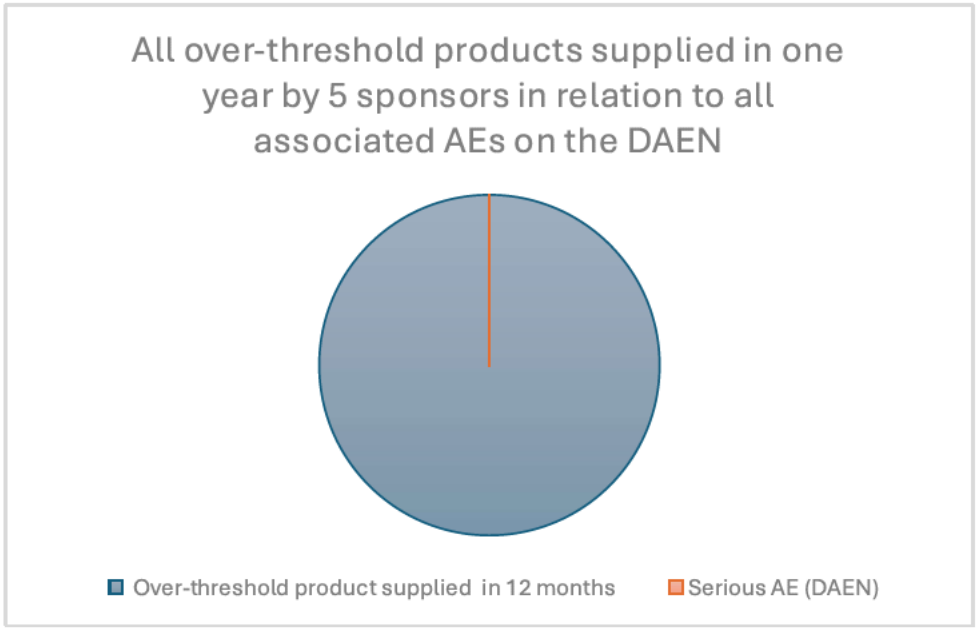
Size Thresholds & Label Requirements	Comments
Option 1 (supported)	
No size thresholds or labelling requirements selected until Sep 2026, after greater data analysis is conducted to ensure a size threshold policy is justified by stratified data that accurately determining the increase in risk in both Listed and Registered OTC medicines.	See Problems 1, 2 & 3. Further, that consumer testing is used to verify need of any labelling elements that are in excess to minimal fundamental changes.
Option 2 (supported & preferred) – Data-driven improvements of appropriate impact	
For the period of 2025-2027, only using size thresholds that are supported by the data available per Problem 3.	An achievable, fair, data-led regulatory impact within the time period proposed.
Round tablets: >12.8mm diameter to be equivalent to high volume Registered medicines (with >5x the sales volumes of all top ten Listed medicines combined) that are also this size and will be exempt. For the Sep 2026 TGO, other sizes should be examined, such as >11.4 diameter, for ALL medicines.	This captures all round Listed medicine tablets that are *larger* than the median common paracetamol brands of 12.8mm that have at least 5x the sales volumes of all top ten Listed medicines combined.
Oval/Oblong tablets: >23.0mm and **>11.0mm**	See justifications for all in Problem 3. 00EL could be considered for Sep 2026 Labelling Order but only with strong supporting data.
Soft Capsules: >26.0mm and **>11.0mm**	
Hard Capsules: 000 or larger.	
Label Requirements: See response to Q 13/14/16.	
Other approach (not supportable)	
Thresholds lower than Option 2, are selected. This is a major and serious policy change with incomplete data resulting in apparent flaws in policy approach. **Label Requirements:** See response to Q's 13, 14, and 16.	Despite non-support for this proposal, it is critical that if it were to proceed for any reason, a much longer transition period would be required (see Problem 4) to prevent significant burden on industry & environment, and avoid S14 requests.

Problem 4: Amplified Regulatory impact; Transition matters

Considering there are tens of millions of dosage forms produced each year and fewer than 500 reported adverse events associated with Listed medicine large oral dosage forms intended to be swallowed whole since 1971, most associated with only the very largest dosage forms, an impact of approximately 35% of all Listed medicines is excessive. It is also critical to consider in the reading of Problem 4, 5, and 6, that each dimension and each additional label element creates a compound effect, markedly amplifying the total impact.

The following example provides an insight into the perspective of sponsors. Six CMA sponsor members who between them have 433 Listed medicines with tablets and capsules exceeding the threshold dimensions, supply in excess of 989 million of these dose forms annually. Adverse events associated with swallowing or product size dimensions over all years totalled just 60.

Figure 11. The proportion of choking related adverse events associated with over-threshold medicines in relation to the number of these products supplied by five sponsors in one year[20]



The calculation on the above figure is 0.06 chance in a million *if* all of the AEs had occurred within a single year. However, those reactions occurred over numerous years indicating the reaction rate is significantly lower and very likely much less than 1 in a billion.

[20] Refer Appendix I

With the current TGA proposals requiring a labelling change for a significant proportion of Listed medicines (approximately 35%), this creates a substantial work load for most stakeholders with products on the market, some of which have multiple SKUs[21], that simply cannot be implemented in the proposed 2-year transition period from regulatory and physical resourcing perspectives.

In particular, it will have greater impacts on small to medium business enterprises who are often relying on contract label manufacturers (rather than inhouse capabilities), and contract labour in order to include and assess the compliance of each label to be updated. These contractors/consultants are subject to availability and material constraints that are out of the control of the affected medicine sponsors. This will create a bottleneck for contractors – whether contract manufacturers, print agencies, ad agencies, consultants etc – resulting in a great deal of stress and potential non-compliance through a practical inability to comply. Due to the large number of medicines captured by the TGA's proposal, a number of sponsors have estimated that only half of the affected products in their portfolios are able to be manageably updated in 2 years without significant impact.

In the transition from TGO 69 to TGO 92, the TGA's 2016 Regulation impact statement: General requirements for labels for medicines[22] provided that a survey of industry conducted in early 2014 identified that non-prescription product label changes are less frequent than for registered prescription medicines, and may extend to around 7 years.

In costing the regulatory impact of those proposed changes, the TGA recognised that the primary costs to industry would be associated with the timing of the proposed changes, recognising that the changes may not be in line with the timing of the label changes under a business as usual scenario. The RIS acknowledges that the longer the transition period, the less cost that industry would incur independent of any other label changes undertaken as part of normal business and reduced flow-on cost to consumers.

- The estimated costs for each sponsor to implement the changes is between $60,000 to approximately $1.5 million.
- The estimated cost of the labelling changes per stock keeping unit (SKU) is between $650 - 10,000. Sponsors with smaller portfolios report higher estimated costs per SKU. IF 35% of products are affected, there are far greater impacts as many products have two or even three SKUs (package options) per ARTG listing.

[21] See Appendix J

[22] Regulation impact statement: General requirements for labels for medicines V3.0 June 2016

- Shipping costs will increase following an increase in packaging sizes to accommodate the addition of new label information, including the number of pallets required, shipping containers and warehousing, (especially for highly temperature sensitive products).

The additional likelihood of further required labelling updates coinciding when the September 2026 Labelling Order comes into effect will result in major changes only a few years apart, imposing additional and significant resource burden on sponsors.

It is reasonable to consider that rather than the inclusion of more information on the already restricted space of most listed medicine labels, some sponsors may choose to reformulate products instead, however this takes longer than 2 years due to the large project management and manufacturing resources required if more than a few products are affected.

It is assumed that a longer transition period is considered by the TGA to potentially result in a delay to immediate benefit to public safety, hence the earlier consultation on this issue. However, we note that reports of AEs for listed medicines have significantly reduced in 2023-24, with more reports attributed to registered medicines. We also reiterate that at least 197 of the reported choking related AEs were for 31 medicines that are no longer on the ARTG.

Manufacturer impacts

Manufacturers estimate that the proposed changes will impact around 37% of their portfolios (by product), or higher where the product is sold in several sizes. Hundreds of product specifications and all related quality documents and Enterprise resource planning (ERP) systems will need to be updated, and multiple labels reviewed due to many products having several stock keeping unit **(**SKUs).

The process of finalising updated specifications prior to implementation; and label artwork review and printing can take up to one year for some sponsors to update. Stability trials on larger containers, which are needed to accommodate additional information, will also be required for some products.

Manufacturers have provided that at a minimum under the current proposal, three full time staff are required in quality, regulatory and customer service to coordinate the required changes, which is a very high expense for manufacturers, industry and therefore consumers.

Human Resource impacts

Industry estimates indicate that, depending on the percentage of portfolio affected, anywhere from one full time staff member, to an entire team of people will be required to carry out the changes within a 2 year period.

In particular, contract manufacturers who deal with packaging and labelling will carry a significant proportion of the impact as numerous sponsors will be requiring changes across multiple portfolios simultaneously. It would require dedicated project managers and extra team resources in each of the following areas; quality, regulatory, safety, product development, marketing, supply chain and graphic design.

Once a change is initiated, it can take between 6-12 months for sponsors to approve these changes for each product label.

The significant increase in volume due to a large number of products affected simultaneously will require project management across each umbrella brand. The higher the proportion affected, the more significantly the ability to process all the changes for all products will be impeded. This was seen by both Listed and Registered OTC medicines in the introduction of TOG 92 in 2016, which was over a 4 year timeframe and required a number of extensions to process the changes.

International considerations

As well as national considerations, many products are exported to overseas markets, which presents an additional set of difficulties for labels:

Sponsors will have to apply for variation filings to Australian Listed medicines that are sold overseas (not as export only, which is still common due to some jurisdictional expectations) with numerous overseas regulatory bodies, which can take up to two years to finalise. This is in addition to the time to redesign, review and print new products labels; a minimum of 6 months.

Impact on Advertising and Online Purchasing

The consultation and draft guidance implies, but does not state, that the proposed 'Warning – Large Tablet' statement would be required to be included in all online advertising, where an advertisement directly facilitates the purchase or other supply of a medicine and the medicine is not able to be physically inspected before purchase. The requirement to change all affected advertisements, including those appearing in numerous online pharmacies and retailers in such a short period, significantly compounds the costs and time-frames.

Similarly, the consultation and draft guidance has not made it clear whether the requirement to display an image of the dosage unit that is true to size with the words 'actual size', would or would not be captured by the meaning of 'health warning'[23] and therefore, whether it would be required to be displayed on online advertising.

Adding a true-to-size image in an online version will not be feasible due to screen differences. It could not reasonably be implemented by advertisers, nor screens adjusted with any surety or reliability by consumers if it were, introducing the risk of consumers misunderstanding information prior to purchase. Consumers Health Forum of Australia (CHF) identified the provision of easy-to-understand Information in the top 5 attributes of information about medicines that is sourced online (2020a).

Unless it is made clear that it is excluded, it could be interpreted by some stakeholders, or by TGA officers that it is required in the future.

Environment and Sustainability Impacts

The requirement to add more information on labels of Listed medicines will result in the need for increased label space that will result in increased packaging sizes for those medicines which are usually presented in a smaller container size. This significantly increases the impact on the environment and sustainability, due to the unnecessary increased use of glass, plastic and labels.

Further, an increase in raw materials needed to produce packaging increases resource consumption and manufacturing emissions; carbon emissions are increased due to the fuel required to transport larger and heavier packages. In addition, the disposal of labels, packaging and marketing materials and technical manuals further contributes to environmental impacts.

CMA has also received member feedback that shipping costs will increase following an increase in packaging sizes to accommodate the voluntary addition of new label information, including the number of pallets required, shipping containers, warehousing, (especially for highly temperature sensitive products).

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[23] ***health warning,*** in relation to a medicine (or an ingredient contained in the medicine), means a warning, contra-indication, precaution or restriction, that is: (a) required under a relevant instrument to be included on the label of the medicine; and (b) reasonably necessary to inform a decision of a consumer to purchase the medicine.

Notably, while sponsors make best efforts in their forecasts to reduce waste and maximise efficiencies, if sponsors will be required to update labels again following the update of TGO 92, additional environmental and sustainability impacts will be again observed in this second round of 'doubled up' label changes with tight compliance timeframes.

Most packaging is made from finite virgin materials due to TGA limits on impurities. In Australia in 2020–21, 6.74 million tonnes of packaging was placed on market; and 44% of this packaging was disposed to landfill[24]. The Australian Government is actively trying to work towards reduced plastic consumption and waste, including by:

- working with all governments and industry to reform the regulation of packaging by 2025, to ensure that all packaging available in Australia is designed in line with circular economy principles;
- supporting industry to achieve the 2025 National Packaging Targets; and
- supporting 20,000 small to medium-sized businesses to use the Australasian Recycling Label and improve their packaging sustainability[6].

The proposed short 2 year transition will create the need to dispose of a large number of plastic labels, and some packaging due to increased packaging and labelling for some listed medicines, is a high plastic wastage scenario counter to these goals.

[24] Department of Climate Change, Energy, the Environment and Water: A circular economy for packaging in Australia

Question 13, 14, 16 – Determining appropriate warning statements and label elements

13. Is the word 'Warning' needed as part of the proposed label statement to alert consumers that a dosage unit is large and presents a risk? Please explain your answer. Please ensure you read Appendix F and submit evidence to support your proposal.
14. Please tell us if you have any other comments about the proposed required warning statement.
16. For large dosage forms, would dimensions of the dosage unit in millimetres (mm) in place of an 'actual size' image on the label be enough to inform consumers about size if dosage units can't be seen through the packaging? Please explain your answer. Please refer to Appendix F for further discussion about this.

The proposed requirements include 4 different label elements that are all required to be grouped together:

A. 'Warning'
B. 'Large Tablet' or 'Large Capsule'
C. 'Actual Size'
D. True to size image (or a potential alternative of mm size dimensions)

Problem 5 – Four label elements are high impact, not evidence driven

The addition of all four elements add high regulatory impact for label space to smaller pack sizes as well as cluttered label information for consumers. As discussed previously, the impact on label space is high. Label real estate is extremely limited for many products and is being increasingly encroached on by rising levels of requirements across the Labelling Order and additional label or warning requirements. Regulators often appear to dismiss this view when it is a real and genuine concern that needs to be taken seriously especially in the environment of ever-increasing label information and warnings.

These proposed changes specify a large amount of high impact label information that does not fit on some labels; creating significant differences between labels. Any proposed labelling requirements needs an approach that can be acceptably incorporated into the presentation of a label, especially where it proposed to include imagery and only affects some, but not all products within an umbrella range.

It is especially a problem for smaller containers that have less space to display information. This significantly increases the impact on the environment and sustainability due to the unnecessary increased use of glass, plastic, and labels (discussed further in Problem 4), and on industry through having to conduct new stability trials on larger containers, which is a high impact cost.

As noted above in Problem 1, the Government's Regulator Performance Guide includes risk based and data driven regulation as a best practice principle; and under this principle, expects regulators to seek to impose the least burden on those that are regulated, while maintaining essential safeguards[25].

Including *all* proposed elements, compounded by the requirement to be in proximity on the label, create maximum impact, and have not been driven by data as a necessity for adequate consumer comprehension.

Consumer testing

This remains a labelling proposal that has not been considered nor implemented anywhere else in the world by any comparable regulator. There are numerous challenges and problems with the proposed labelling requirements, as outlined in Problem (ZC) below. Consumer testing associated with larger dosage units and the proposed multi-element solutions has not been undertaken. Consumer testing is the minimal necessity to understand and try to resolve the different problems and possible solutions.

Such testing would need to consider each element alone and in combination, , to establish the most effective and lowest impact regulatory option between consumer understanding and sensible label requirement. If the addition of an element has, in fact, no additional benefit, then it does not need to applied to the label.

Like any study, it is critical that the study investigates a range of options that are presented in a way that is unbiased towards seeking any one outcome, and is accurate to existing label conditions where a great deal of other information is present – often in a very limited space.

[25] https://www.finance.gov.au/government/managing-commonwealth-resources/regulator-performance-rmg-128/principle-2-risk-based-and-data-driven

Problem 6 – Cluttered information and Consumer understanding

Equally importantly, an excess of information, too many statements and cluttered information is likely to overload consumers, leaving them unmotivated to read or try to understand the information (Geuens et al., 2021). Crowdedness of a label, including a lot of information in a relatively limited area, is significantly related to behavioural compliance; and an increase in clutter on a warning has been shown to induce a lower level of behavioural compliance to that warning (Hanock et al., 2020).

It applies not only to these proposed statements, but to the combination of these with all other existing warnings and relevant information on a label. Consumers are advised to 'always read the label' however, the label needs to be sufficiently succinct so that consumers have the time and patience to both read and comprehend the totality of label information. Consumers Health Forum of Australia (CHF) provided that regardless of how consumers accessed information on medicines, it was crucial that it was clear, easy to read and easy to understand (2020b). Thus, each label element and word requires scrutiny to assess whether the need is there.

1. Use of the words 'Actual size / Size' and/or 'Large [dosage form]

As the first example, use of both elements 'actual size' *and* 'large tablet' in proximity to an image of the dosage form communicates the same information, in slightly different ways, which is excessive and unnecessary.

The word 'actual' in 'actual size' is additionally unnecessary, as an image of the dosage form together with the word 'size' is sufficient to communicate the message. Regulators and courts rely upon common meanings, using the Australian Macquarie Dictionary as the main definition, which relevantly for 'size' is:

- 'the dimensions, proportions, or magnitude of anything'

Further, use of the word 'size' next to an image of a tablet or capsule without requiring additional cluttered elements on premium label space, specifically the words 'Actual size' or for larger dosage forms 'Warning' or 'Large tablet', as confirmed by member feedback, provides an increased incentive for industry to voluntarily implement an image with the word 'size' across an umbrella brand. This enables consumers greater ability to compare multiple product types.

2. Use of the word 'Warning'

The consultation canvassed opinions in favour of the view to include the word 'warning', and did not provide an unbiased overview of evidence for and against. The Government's Regulator Performance Guide provides principles for decision-making that are data-driven rather than opinion-led.

The balance of evidence supports that use of the word 'warning' in this circumstance will be detrimental to the safety of sensitive consumers, rather than beneficial. Considering the use of the word is unnecessary in context of use of either 'size/actual size' or 'large tablet/capsule', it represents an unacceptable risk to add an unnecessary and potentially unsafe signal word.

The word 'Warning' is unnecessary and on balance, an increased risk for consumers:

a) The word 'warning' has the potential to invoke fear and anxiety, which could exacerbate swallowing difficulties. We strongly disagree with the view that this is not a compelling argument to not require the word 'warning'. Research demonstrates that swallowing difficulties are attributed to anxiety and on the balance of evidence, specifically in regards to swallowing ability, the use of the word 'Warning' is demonstrably more detrimental to the safety of sensitive consumers than beneficial.

   The findings of Schiele et al. (2013) demonstrate that inducing anxiety is a director contributor to swallowing problems:

   - of the 296 patients who reported they were afraid of taking tablets and capsules, 93 (31.4 %) considered their anxiety a reason for their swallowing problems;
   - 221 of 1,051 participants (21.1 %) mentioned their aversion to drug intake; and a further 206 (19.6 %) explained their problems with previous bad experiences. Patients who mentioned aversion to drug intake as a 3reason for their difficulties also reported anxiety (28.9 %) as an additional cause.

   Evidence of greater risk is summarised below:

   – A perceived physically threatening situation induced by a warning can trigger anxiety and contribute to difficulty swallowing solid oral dosage forms (Dorman et al., 2017).

- Fluoroscopic studies have shown that patients experience oesophageal spasm when prompted to recall unpleasant topics, illustrating that the potential role of anxiety must be considered, even when anxiety is not the primary presenting problem (Kaplan et al.,2010).
- 'Pill aversion', the physical or mechanical difficulty with swallowing pills with no persisting medical cause, can be associated with anxiety (Dorman et al., 2017; McCloskey et al., 2022).
- Swallowing solid oral dosage forms can be perceived as an unpleasant experience, and some individuals may become anxious at the time of administration (Seedat & Zayannakis, 2020; Radhakrishnan et al., 2021).
- Oesophageal hypervigilance and visceral anxiety were the strongest predictors of dysphagia severity (Carlson et al., 2020). Anxiety is also associated with oesophageal bolus perception among otherwise asymptomatic, healthy subjects; and focused attention on oesophageal sensations, heightened anxiety, expectations of discomfort, all contribute to oesophageal hypervigilance and associated hypersensitivity (Carlson et al., 2020).
- Anxiety and negative associations with swallowing a dosage form is likely contribute to swallowing difficulty (Kerins, 2020).
- A previous issue when swallowing medication can lead to anxiety when taking medication (Radhakrishnan, 2016; Seedat & Zayannakis, 2020).

b) If the label displays 'Size/Actual size' or 'Large tablet/capsule' next to the required image, this messaging adequately communicates that the dosage form is large, alerting consumers who are sensitive to size and swallowing considerations to the risk; there is no imminent or verified need for the word 'warning'.

c) Research has demonstrated that the more often a warning is encountered, the less likely the person will notice it on subsequent encounters (Wogalter, Conzola & Smith-Jackson, 2002). This effect may be due to desensitisation because of the frequency with which warnings are encountered (Ebert, Ackermann & Bearth, 2022), some of them obvious, across a range of therapeutic and non-therapeutic goods; and the failure of some warnings to distinguish between large and small risks. The current proposal is failing to distinguish between small and large risks by applying the proposal to ~35% of the marketplace on average. This dilutes the impact and usefulness of the warning for

consumers and reduces the likelihood that consumers will pay attention to the information. The extremely low level of risk of a large percentage of products currently captured by the proposal is represented in our earlier data.

d) The word 'Warning' is accepted as unnecessary on consumer goods presenting a similar level of risk. In Australia, it is common practice that consumers are familiar with, for precautionary and warning statements that are intended to warn the consumer, the word 'warning' not being included. Whether a statement is designated as an 'advisory' or 'warning' statement, neither are required to use the word even for higher risk situations such as propolis allergy or unpasteurised milk products. This is outlined by the FSANZ webpage[26] and Part 1.2 of the Food Standards Code legislation[27].

From a policy perspective it would seem reckless to introduce an unnecessary word when there is sufficient balance of evidence that this word will enhance the risk trying to be avoided.

3. Is a true-to-size image or a mm dimension required?

There are numerous problems with implementing an image as outlined below, all of which minimally require careful policy consideration and consumer testing.

a) Many OTC medicines[28] have an image on the bottle that is <u>not</u> true to size, usually on the main (front facing) label. This proposed requirement reflects an unjustifiable inconsistency in the approach to consumer safety between Listed and Registered medicines of the same dimensions. It creates significant confusion for health professionals and significant misunderstandings and misinformation in the consumer marketplace. This will lead to inappropriate purchases on the basis of that misunderstanding. The ability to do this may create an incentive for other Registered

[26] FSANZ webpage 'Warning and advisory statements'; accessed 15 July 2024 https://www.foodstandards.gov.au/consumer/labelling/advisory

[27] FSANZ webpage 'Food Standards Code legislation' & relevant links accessed 15 July 2024 https://www.foodstandards.gov.au/food-standards-code/legislation

[28] Examples include: [redacted]

and Listed medicines to increasingly include images that are not true-to-size on the label, further compounding the problem.

b) Under the current proposal *all* Registered medicines and around 60% of listed medicines will not have any information at all, therefore there is no way for consumers to compare the size of large tablets/capsules using either the image or mm information.

c) A sponsor who started adding the warning to labels voluntarily in anticipation of requirements being implemented without an adequate transition time, has had feedback from their practitioner customers, their clients, and sales representatives, that the outline of the dosage form on the container gives a false impression of the actual size i.e., that it looks much larger than it actually is, even though the dimensions are correct. When the container is opened, they find the dosage forms are of an acceptable size to be swallowed, and not as large as they had expected based on the label information. Whether this is an optical issue or a result of other factors such as curvature of the bottle is not yet understood. However, it indicates the necessity that consumer testing is conducted to fully understand if the labelling approach creates appropriate consumer expectations that are equivalent to the size of the actual dosage form, and whether there are other factors influencing this.

d) All small, and many medium, containers (especially those such as multivitamins) do not have the label space to include the actual size dimensions (as well as the large number of warnings). This markedly increases industry through packaging changes that require new stability trials, and environmental impacts as discussed earlier. Including mm sizes for small-medium containers reduces the impact for smaller containers to some extent, but remains plagued by the aforementioned issues.

   Note: For containers holding large dosage forms, a small-medium container generally contains less than 100 tablets or capsules, and large containers generally contain 100 or more dosage forms.

Lowest Impact Labelling Requirements to Achieve Outcomes

CMA propose low impact approaches that align with the principles for providing clear information and minimising visual clutter on medicine labels, which is crucial for consumer safety and comprehension, and the reduction of medication errors.

Including only the information 'Large Tablet' or 'Large Capsule' is the minimum impact option under the principles of the the Government's Regulator Performance Guide and that is appropriate, especially on small and medium containers, due to the amount of information already displayed and therefore, the limited label space on most Listed and Registered OTC medicines. This approach does not include actual size information via an image or mm dimensions: Use of 'large tablet' or capsule alone creates a differentiation between two different labels, **sufficient to provide transparency to consumers for their product selection**.

Notably, it is equivalent to the kind of approach commonly taken by FSANZ through transmitting essential label information without creating excessive clutter or non-supportable impacts.

In their discussion on the application of attention maintenance to pharmaceutical labels, Wogalter & Sojourner (1999) provide that the allocation of different information components to different parts of the medicine label permits brevity, thereby increasing people's willingness to read what is there (Wogalter & Sojourner, 1999).

Unless the minimum impact option is chosen, neutrally-worded consumer testing needs to be conducted, using wording that does not, or is not intended to, induce bias in the participants.

Label mock-ups

Consultation option:

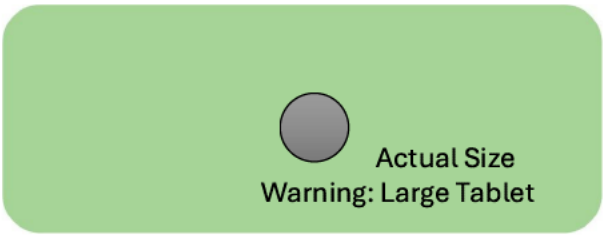

Image affected by curvature of the container

This option demonstrates excessive label real estate and impact, with more information than necessary to inform. The curvature and optical issue has the ability to mislead on actual tablet/capsule size.

Lowest impact change creating an adequate differentiation between products:

The following options are sufficient to convey the message and are minimal impact and are aligned with Regulator Performance Guide, FSANZ warning statements, and some other TGA advisories.

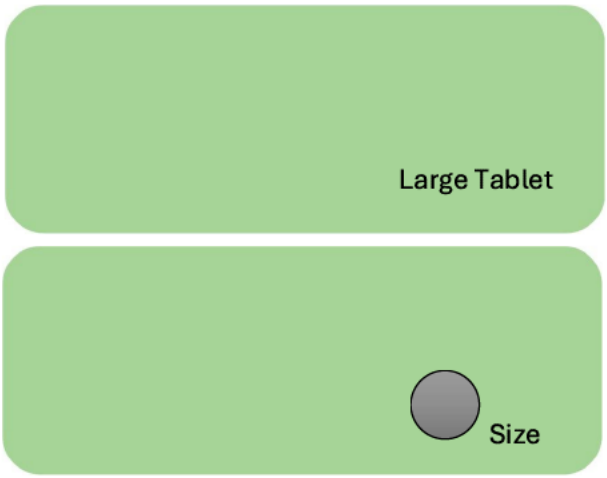

Image affected by curvature of the container

The following regulatory impact offset options for sponsors should be available:

a) A cap sticker or label that is securely affixed to the lid of the medicine container, or printed onto the lid during the packaging step of manufacture, that depicts an actual size image of the dosage form.

We note the consultation paper states the number of choking related cases reported to the TGA for each age group (where age was reported) shows that most reports involved consumers 65 years and over, while the highest number of reports of any group was for 75 years of age and over. This higher incidence of choking events among older adults is also reflected in the broader literature. The results of a small study by Wogalter & Dietrich (1995) on enhancing label readability for over-the-counter pharmaceuticals by elderly consumers found that older participants (mean age 75 years) judged medicine containers with an added cap label, which made the printed material easier to notice and read, more positively than containers without the cap information. This suggests that a cap sticker, or cap label, may provide a useful and accessible source of information, particularly for older adults who are at greater risk.

b) If the 'Large tablet/capsule' statement applies, it should be permitted to be grouped with other warnings (where they are required) for ease of finding information; or grouped with the directions for use, where no other warnings are required on the medicine label.

Question 15 – Directions for Use

For large oral dosage forms, should alternatives to the directions 'Swallow with water' be allowed if they have a similar meaning? For example: 'Take with fluid'. Please explain your answer. If you think similar directions should be allowed, do you think there should be a list of acceptable directions that sponsors can choose from to display on the label? Please see Appendix F for further discussion about this.

CMA supports the ability for sponsors to have the flexibility to use acceptable alternatives to the proposed directions 'Swallow with water' if they have a similar meaning. For example:

e) Take with fluid (or words to that effect)
f) Take with water (or words to that effect)
g) Take with liquid (or words to that effect)

'Fluid' and 'liquid' should be permitted as an alternative to 'water'. The use of thickened liquids is a management strategy for individuals with swallowing difficulties and dysphagia (Barbon & Steele, 2018; Cichero, 2013; Newman et al., 2016).

These options, including (or words to that effect) provide flexibility for sponsors, who may wish to select a statement appropriate to their particular type of dosage form, or population.

Question 17 - Guidance

Do you think the proposed guidance in Appendix G to support the proposed new requirements for large dosage forms is clear and easy to understand? Please explain your answer.

The TGA proposed guidance provided in Appendix G of the consultation paper has not considered stakeholder feedback yet to be received as part of the consultation, unfortunately suggesting that the decision has already been made and that the basis for the consultation is not genuine.

Interaction with industry based on their consultation feedback should continue, before a decision is finalised, and when a final decision that strikes the right balance is found, we welcome targeted consultation on proposed guidance.

Packaging that allows one entire dosage unit to be seen

The consultation proposes that an alternative to the label image of a dosage unit is if at least one entire dosage unit is visible through the packaging.

The proposed guidance provides that this includes tinted packaging where a dosage unit can still be seen through the packaging around or through the label, or when viewed through the bottom surface; but does not include packaging where an opaque label takes up most of the space, for example on a bottle, where a single whole dosage unit cannot be seen when looking through the bottle around the edges of the label and also cannot be seen through the bottom of the bottle.

CMA recognises that impact could potentially be reduced for some sponsors under this option. However, we hold concerns over the potential differing interpretation of this guidance between TGA assessors and subsequent potential allegations of non-compliance if this is written into TGO 92 legislation. As such, CMA seeks confirmation from the TGA that using glass bottles (including tinted glass and small glass containers) will guarantee that sponsors are not required to include an image of the dosage form on the label.

Question 18 - Other comments

Please tell us if you have any other comments about the proposed new labelling requirements for large solid oral dosage forms intended to be swallowed whole.

Coated dosage forms

While the TGA acknowledges that the use of coating materials and the texture of a dosage form can make it easier to swallow, these factors are not recognised in the TGA's proposals. Therefore, a significant proportion of oral listed medicines are likely to be captured where the risk profile is actually reduced due to the use of coatings. This policy approach reduces industry's incentive to spend increased resources and costs on improved coatings, when it should be encouraged.

The FDA guidance (2022) provides that physical attributes of tablets and capsules should be considered in the context of their effect on ease of swallowing, including the presence and composition of a coating, which can affect the ease of swallowing tablets or capsules. The guidance also notes that the lack of a film coating can decrease or prevent tablet mobility compared with a coated tablet of the same size and shape. The EMA Reflection paper on the pharmaceutical development of medicines for use in the older population (2020) also suggests coated tablets are easier to swallow for older adults.

We have previously provided that various dosage form coating technologies that are demonstrated to reduce choking risk (Drumond & Stegemann, 2022; Ershad et al., 2021; Kerins, 2020; Overgaard et al., 2001; Hofmanová et al., 2019; Kelly et al., 2010; Notenboom et al., 2017; Phillips et al., 1992). Certain coatings are known to enhance slipperiness and therefore, improve swallowability (To et al., 2017), including in individuals aged 18 to 75 years of age (Hofmanová et al., 2019). CMA has received sponsor information that, following product reformulation to include film-coating on a medicine that previously received AE reports, none have since been reported.

Many of the paracetamols and other OTC medicines tested in the sampling exercise were uncoated tablets. Conversely, the [redacted] 11.3mm round coated tablet with an "Easy to Swallow" label claim[29] is an example to illustrate that film coatings are considered easier to swallow by TGA, to the extent it can be marketed as such, including on tablets of a larger diameter than the current proposals for listed medicines. A similar policy recognition for coated listed medicines would acknowledge the work of product development teams who take such

[29] [redacted]

matters into consideration, and incentivise the expanded use of coatings and textures that improve swallowability.

TGA education

CMA notes and supports the TGA in improving consumer education through their commitment to provide educational material for consumers, especially older adults on safer swallowing techniques through online forums (for example as a web statement and on social media), provided that this information is not limited to Listed medicines in a biased way. Comparable regulators who provide education on this issue refer to pharmaceutical medicines, and as already demonstrated in this submission, there is good evidence Registered medicines are similarly affected across the prescription and OTC spectrum.

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APPENDIX A: Registered OTC medicines exceeding thresholds (Footnote 9)

Table 1. 31 Registered medicines from a sample of 48 available for self-selection in pharmacy and/or supermarket exceeding proposed large tablet/capsule labelling dimensions

	[redacted]	% exceeding proposed limits
1		43
2		42
3		42
4		42
5		42
6		42
7		42
8		41
9		38
10		38
11		37
12		33
13		33
14		29

15	[redacted]	26
16		24
17		24
18		19
19		18
20		17
21		17
22		16
23		14
24		14
25		12
26		11
27		11
28		7
29		3
30		2
31		2

*measured with digital calipers to closest 0.1mm, unless in (brackets) – measured to closest 1mm with ruler.

Appendix B: Data for Figure 4

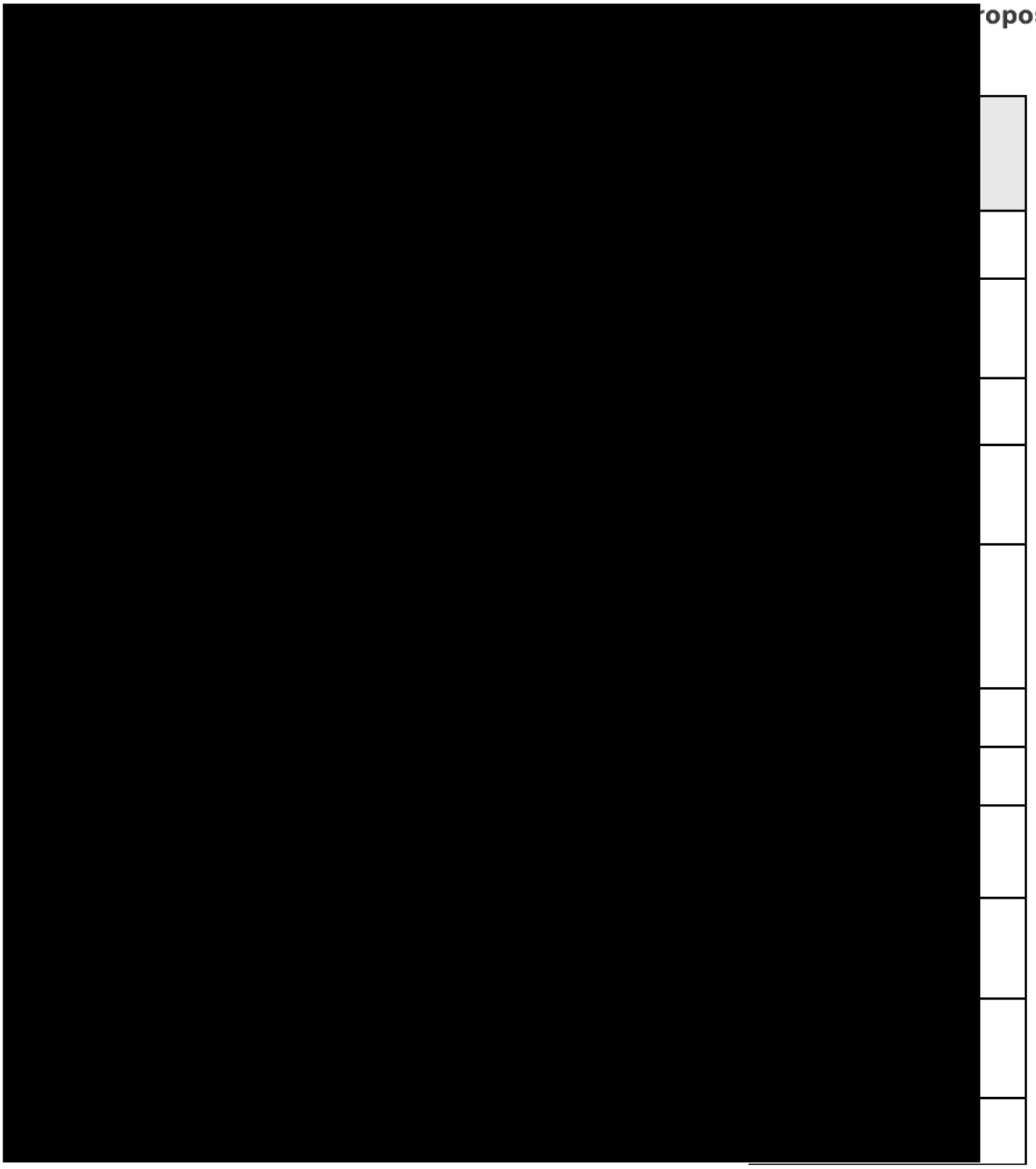

Table 2: Top 10 Listed Medicines by Sales Volume – IQVIA Scan Total Pharmacy and Grocery (Coles & Woolworths), Unit Sales for 52wks ending 15 June 2024.

Top 10 listed medicines by sales volume	Sales volume (Not separated by pack size)
[redacted]	[redacted]

Appendix C: Data for Figure 5

Ten sponsors provided information about the percentage of their product portfolio was sized above the proposed threshold dimensions.

Table 1. Sponsor information on percentage of affected portfolio impacted by the proposed threshold dimensions.

Sponsor deidentified for confidentiality	% product portfolio below threshold	% product portfolio above threshold
[redacted]	[redacted]	[redacted]

Details of dose forms associated with product size reports or consumer complaints were provided by three sponsors. Table 2 provides the details of the dose forms and dimensions.

Table 2. Dosage forms and dimensions associated with adverse events

Product – key ingredient or purpose	No. of size AEs	Length (mm)	Width (mm)	Dosage Form
[redacted]	1	23.1	10.4	Coated tablets
	1	22.6	10.4	Coated tablets
	1	24	10.5	Coated tablets
	4	21.5	9.5	Uncoated tablets
	2	23.1	9.9	Coated tablets

2	18.6	10.1	Oval film coated tablet
3	23	10.3	Oval uncoated tablet
3	23.4	10.7	Oval film coated tablet
1	23	10.3	Oval uncoated tablet
1	22.5	11.3	Oval tablet
1	18.7	10.2	Oval film coated tablet
3	23.4	10.8	Oval coated tablet
1	23.5	11	Oval film coated
1	20.4	10.4	Oval coated tablet
2	18.7	10.2	Oval film coated tablet
7	22.6	11.4	Oval film coated tablet
1	20.4	10.4	Oval tablet
1	18.8	10.4	Oval film coated tablet
5	23.5	11	Oval film coated tablet
39	23.5	11	Oval film coated tablet
2	23.15	10.4	Oval film coated tablet
1	24	10.9	Film coated tablet
1	24	10.9	Film coated tablet
2	22.7	9.7	Film coated tablet
2	24	11	Film coated tablet
1	22.7	9.7	Film coated tablet
1	22.7	9.7	Film coated tablet

Appendix D: Data for Figure 6

These numbers were derived when the size of product could be determined using either DAEN information or information provided by sponsors.

Table 1. Total number Adverse events for 1000mg; 15000mg; 2000mg marine omega oils currently on ARTG that are all over the proposed size thresholds for capsules

Formulation	AEs 1000g (1g)	AEs 1500g (1.5g)	AEs 2000g (2 g)
omega-3 marine triglycerides/ docosahexaenoic acid; eicosapentaenoic acid; omega-3 marine triglycerides	**1**	**5**	**134**
Euphausia superba oil	**2**	**1**	**8**
TOTAL	**3**	**6**	**142**

Based on products with serious and non-serious AEs [DAEN data + (Sponsor data from 3 sponsors of 2000mg fish oil – minus any duplications from DAEN data)], where the quantity of active ingredient oil in the product was able to be identified.

Appendix E: Data for Figure 7

By Sales Volume – IQVIA Scan Total Pharmacy and Grocery (Coles & Woolworths), Unit Sales for 52wks ending 15 June 2024.

Based on currently supplied products with serious and non-serious AEs [DAEN data + (Sponsor data from 3 sponsors of 2000mg fish oil – minus any duplications from DAEN data)], where the quantity of active ingredient oil in the product was able to be identified.

52 weeks Sales Volume vs all Adverse Events to 19 Feb 2024 for 1000mg, 1500mg & 200mg marine oils

Table 1: 1000mg

Name	Total unit	AEs
[redacted] CAPSULES 1000 MG	338620	1
[redacted] CAPSULES 1000 MG	261771	
[redacted] CAPSULES 1000 MG	239651	
[redacted] CAPSULES 1000 MG	166164	
[redacted] S CAPSULES 1000	157280	
[redacted] CAPSULES 1000 MG	137798	
[redacted] CAPSULES 200	132923	
[redacted] CAPSULES [redacted] 1000 MG	54109	1
[redacted] 1000 MG	51520	
[redacted] 1000 MG	51437	

Table 2: 1500mg

Name	Total unit	AEs
[redacted] CAPSULES 1500 MG	286343	1
[redacted] CAPSULES 1500 MG	202714	2
[redacted] CAPSULES 1500 MG	106091	0
[redacted] CAPSULES [redacted] 1500	78404	0
[redacted] CAPSULES 1500	74122	0

Table 3: 2000mg

Pack long name	Total unit	AEs
[redacted] CAPSULES 2000	134916	8
[redacted] 2000 MG	108509	0
[redacted] 2000 MG	43550	0
[redacted] CAPSULES 2000	35551	2
[redacted] CAPSULES 2000 MG	45963	6

Appendix F: Data for Figure 8

Table 1: 00EL Hard Capsules

Sponsor ID	No. of 00EL products	Swallowing related AEs /complaints
[redacted]	2	0
	1	0
	1	1
	42	1
Total	**46**	**2**

Appendix G: Data for Figure 9

Table 1: Adverse events in oval and oblong tables by length

Length	22.0-22.4	22.5-22.9	23.0-23.4	23.5-23.9	24.0-24.4
Adverse Events	0	13	7	45	5

Based on data from 3 sponsors

Appendix H: Data for Figure 10

Table 1: Adverse events in oval and oblong tablets by width over 9mm

Width	9-9.4 mm	9.5-9.9 mm	10- 10.4 mm	10.5 - 10.9 mm	11-11.4 mm
Adverse events	9	6	15	9	55

Based on data from 3 sponsors.

Appendix I: Data for Figure 11

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

[redacted]

Appendix K: Examples of Dosage forms exceeding 23.3mm L and/or 9mm wide with Nil AEs or complaints to sponsors

Note that a limited selection was available as this information was requested late in the consultation period.

Table 1. Soft gel exceeding 23.3mm L and/or 9mm wide with Nil AEs/complaints

[redacted]	No. of choking related reactions	Length (mm)	Width (mm)	Dosage Form
	Nil AEs and nil complaints	26mm	10mm	Softgel capsule
	Nil AEs and nil complaints	26mm	10mm	Softgel capsule
	Nil AEs and nil complaints	26mm	10mm	Softgel capsule
	Nil AEs and nil complaints	26mm	10mm	Softgel capsule
	Nil AEs and nil complaints	26.5	9.9	Capsule, soft
	Nil AEs and nil complaints	16.39	9.25	Capsule, soft
	Nil AEs and nil complaints	27.4	9.9	Capsule, soft
	Nil AEs and nil complaints	26.22	8.93	Capsule, soft
	Nil AEs and nil complaints	26.6	9.5	Capsule, soft
	Nil AEs and nil complaints	27.4	9.9	Capsule, soft gel

Nil AEs and nil complaints	26.5	9.9	Capsule, soft
Nil AEs and nil complaints	16.39	9.25	Capsule, soft
Nil AEs and nil complaints	26.5	9.9	Capsule, soft
Nil AEs and nil complaints	26.6	9.5	Capsule, soft
Nil AEs and nil complaints	25.7	10.1	Soft gel
Nil AEs and nil complaints	25.8	9.2	Soft gel
Nil AEs and nil complaints	25.4	9.3	Soft gel

Table 2. Hard capsules examples exceeding 23.3mm L and/or 9mm wide with Nil AEs/complaints

No. of choking related reactions	Length (mm)	Width (mm)	Dosage Form
Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00
Nil AEs and nil complaints	25.6	8.6	Capsule, hard Size 00EL
Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00
Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00

[redacted]	Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00
	Nil AEs and nil complaints	21.8	7.7	Capsule, hard Size 0
	Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00
	Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00
	Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00
	Nil AEs and nil complaints	23.7	9	Capsule, hard Size 00

Table 3. Tablet examples exceeding 22mm L and/or 9mm W with Nil AEs/complaints

Product	No. of choking related reactions	Length (mm)	Width (mm)	Dosage Form
[redacted]	Nil AEs and nil complaints	23.2	10.5	Film coated tablet
	Nil AEs and nil complaints	23.2	10.5	Film coated tablet
	Nil AEs and nil complaints	23.2	10.5	Film coated tablet
	Nil AEs and nil complaints	23.2	10.5	Film coated tablet
	Nil AEs and nil complaints	23.2	10.5	Film coated tablet
	Nil AEs and nil complaints	10.4	10.4	Tablet, film coated

Nil AEs and nil complaints	10.4	10.4	Tablet, uncoated
Nil AEs and nil complaints	9.5	9.5	Tablet, uncoated
Nil AEs and nil complaints	17.15	9.3	Tablet, film coated
Nil AEs and nil complaints	18.6	10.2	Tablet, film coated
Nil AEs and nil complaints	18.75	10.2	Tablet, film coated
Nil AEs and nil complaints	17.1	9.3	Tablet, film coated
Nil AEs and nil complaints	10.4	10.4	Tablet, film coated
Nil AEs and nil complaints	10.4	10.4	Tablet, film coated
Nil AEs and nil complaints	11.2	11.2	Tablet, film coated
Nil AEs and nil complaints	11.2	11.2	Tablet, film coated
Nil AEs and nil complaints	20.1	20.1	Tablet, film coated
Nil AEs and nil complaints	19.8 - 20.4	19.8 - 20.4	Tablet, film coated

Nil AEs and nil complaints	22.9	10.45	Tablet, film coated
Nil AEs and nil complaints	11.05	11.05	Tablet, uncoated
Nil AEs and nil complaints	10.7	10.7	Tablet, coated
Nil AEs and nil complaints	16.8 - 17.4	9.0 - 9.6	Tablet, film coated
Nil AEs and nil complaints	18.2 - 18.8	9.7 -10.3	Tablet, film coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, coated
Nil AEs and nil complaints	10.1 - 10.7mm (diameter)		Tablet, film coated

Nil AEs and nil complaints	9.3-9.9	9.9	Tablet, film coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	6.35	6.35	Tablet, uncoated

Nil AEs and nil complaints	16.8-17.4	9.0-9.6	Tablet, film coated
Nil AEs and nil complaints	12	12	Tablet, uncoated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	19.8-20.4	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	19.9–20.5	9.9–10.5	Tablet, film coated
Nil AEs and nil complaints	19.8–20.4	9.8–10.4	Tablet, film coated
Nil AEs and nil complaints	19.8–20.4	9.8–10.4	Tablet, film coated
Nil AEs and nil complaints	18.3-18.9	9.8-10.4	Tablet, film coated
Nil AEs and nil complaints	19.8–20.4	9.8–10.4	Tablet, film coated

[redacted]	Nil AEs and nil complaints	20.4	10.4	Tablet, film coated
	Nil AEs and nil complaints	22.4	8.7	Film coated tablet
	Nil AEs and nil complaints	21.9	10.0	Film coated tablet
	Nil AEs and nil complaints	22.3	8.7	Film coated tablet
	Nil AEs and nil complaints	23.9	10.9	Film coated tablet
	Nil AEs and nil complaints	24.2	11.1	Film coated tablet
	Nil AEs and nil complaints	23.0	9.9	Film coated tablet
	Nil AEs and nil complaints	23.5	10.6	Film coated tablet
	Nil AEs and nil complaints	24.2	11.1	Film coated tablet
	Nil AEs and nil complaints	24.1	11.0	Film coated tablet
	Nil AEs and nil complaints	24.0	11.1	Film coated tablet
	Nil AEs and nil complaints	23.9	10.9	Film coated tablet

[redacted]	Nil AEs and nil complaints	23.1	10.0	Film coated tablet
	Nil AEs and nil complaints	22.8	10.1	Film coated tablet