WEIGHTED AVERAGE MONTHLY TREATMENT COST (WAMTC) USERS' MANUAL

APRIL 2009

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PHARMACEUTICAL EVALUATION BRANCH (PEB) CONTACT LIST FOR WAMTC INQUIRIES

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USEFUL WEB ADDRESSES

WAMTC Users' Manual
http://www.health.gov.au/internet/main/publishing.nsf/Content/1A0158FB66F92395CA25738E001627A7/$File/WAMTC%20Guidelines.pdf

WAMTC calculator
click on Excel file at
http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-pricing-wamtc

Price Proposal Template
can be found in WAMTC Manual, as ***Attachment H***

PBPA Policies, Procedures and Methods Manual
http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs-pbpa-policies-contents

PBAC Guidelines
http://www.health.gov.au/internet/main/publishing.nsf/Content/pbacguidelines-index

Therapeutic Relativity Sheets
http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-pricing-therelativity.htm

Medicare Claims data
https://www.medicareaustralia.gov.au/statistics/dyn_pbs/forms/pbs_tab1.shtml

DUSC Guild data for under co-payment prescription numbers
Circulated to responsible persons by PBPA Secretariat with Medicare Australia data and initial WAMTC calculator.

PBS Reform Fact Sheets
http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs_reform_02feb07.htm

GLOSSARY OF COMMONLY-USED TERMS AND ABBREVIATIONS

Across-the-board	The same for all strengths and formulations of a drug eg a 5% across-the-board price reduction would require the DPMQ at each strength and formulation to be reduced by 5%.
Adjusted WAMTC	The WAMTC process involves realigning sample dosage data to reflect the relativities observed between formulations and/or strengths of drugs in combined Medicare Australia script numbers and DUSC under co-payment script estimates, and estimating the average cost per patient to the Australian Government of a month's treatment on this basis. The WAMTC calculated using the sample dosage data is thus adjusted to reflect the known prescription numbers from the Medicare Australia and DUSC data.
Authority required	A restricted PBS listing that requires the prior approval from Medicare Australia (or the DVA) before prescribing by a doctor. In some cases the application must be made in writing.
Benchmark drug	In a WAMTC group, this is the drug with the lowest cost to the PBS, against which the costs of other drugs in the group are compared. The benchmark drug has a WAMTC with the lowest 95% upper confidence bound. In a therapeutic group, the benchmark drug must be available without premiums.
Benchmark price	Each drug has a benchmark price, or set of prices, irrespective of whether it is the benchmark drug. For each formulation and strength of a drug, this is the lowest price to the Australian Government for that PBS item, which is the base price for other brands referenced to it. For a therapeutic group, the product at the lowest price to the Australian Government is the base price for other drugs referenced to it.
Benchmark WAMTC	The actual point estimate of the adjusted WAMTC of the drug that has the lowest 95% upper confidence bound for the WAMTC group.
BP	Brand premium. This is a premium charged by a manufacturer above the benchmark subsidised price of any formulation and strength of a drug or bioequivalent brands, and is paid by the patient.
Co-payment	There are two levels of co-payments. Concessional patients make a small contribution to the cost of a PBS-listed prescription. General patients (those without a concession card) make a greater contribution. Current co-payment amounts can be found in the latest monthly version of the Schedule of Pharmaceutical Benefits (http://www.pbs.gov.au/html/healthpro/home).

Cost Effective	A proposed drug is considered acceptably cost-effective by the PBAC if the Committee considers that, for a specified main indication, the incremental benefits of therapy involving the proposed drug over therapy involving its main comparator(s) justify its incremental costs and harms.
Cost minimisation	A type of economic analysis where the proposed drug is demonstrated to be no worse therapeutically (in terms of both safety and effectiveness) than a listed comparator and the PBAC concludes that it too is acceptable at the same or a lower price.
Data sources	Refers to the origin of data for either script numbers (see Medicare Australia data and DUSC data), or dosage data.
Dosage data	A sample of prescribed daily dosages for each strength and formulation of each drug in a WAMTC group.
Dosage relativity	The relationship of one medicine to others, in terms of dosage, effectiveness etc. Therapeutic relativity sheets, which incorporate the dosage relativity information determined by the PBAC, form the basis of most pricing decisions of the PBPA.
DPMQ	Dispensed price for maximum quantity is the price of a medicine including mark-ups and pharmacist dispensing fees.
DUSC data	The Drug Utilisation Sub-Committee (DUSC) of the PBAC obtains data from the Pharmacy Guild Survey on under co-payment prescription numbers. These are used to adjust sample dosage data numbers to reflect actual prescribing patterns for under co-payment scripts.
DVA	Department of Veterans' Affairs.
Equivalent	A drug which has been accepted as no worse therapeutically than another drug will be considered equivalent to that drug for pricing purposes.
Global test	Chi-square test (based on assumed underlying normal distributions) for equality of all adjusted WAMTCs.
GMiA	Generic Medicines Industry Association.
Medicare Australia	Medicare Australia (formerly the Health Insurance Commission, HIC).
Medicare Australia data	Prescription numbers from the Medicare Australia website (https://www.medicareaustralia.gov.au/statistics/dyn_pbs/forms/pbs_tab1.shtml). Used to adjust sample dosage data numbers to reflect actual prescribing patterns among the different strengths or formulations of each drug. Does not include under co-payment script numbers – see DUSC data.
MA	Medicines Australia.
Pairwise comparison	Test (based on assumed underlying normal distributions) to determine whether there are statistically significant differences between two WAMTC estimates. Compares each drug's WAMTC with that of the benchmark drug.
PBAC	The Pharmaceutical Benefits Advisory Committee.

PEB	The Pharmaceutical Evaluation Branch, of the Department of Health and Ageing.
PBPA	The Pharmaceutical Benefits Pricing Authority.
PBS	The Pharmaceutical Benefits Scheme.
PBS Item	A particular form and strength of a drug covered by a unique PBS code.
Point estimate	The actual WAMTC for a drug (not a confidence bound). Drugs with a WAMTC significantly different from that of the benchmark drug after pricing proposals are received must reduce prices to match the exact WAMTC of the benchmark drug (i.e. the point estimate).
Point-to-point reduction	The WAMTC of the drug in question must reduce to match, exactly, the WAMTC of the benchmark drug (the point estimates must be the same). This is achieved through either across-the-board price reductions, or for sole suppliers through possibly some variation in reductions across different strengths/formulations.
Pre-calculation file	The WAMTC calculator with all required dosage and pricing data entered into the appropriate spreadsheets. This is prior to activating the calculator. A saved version of the pre-calculation file will enable the user to re-open and re-run the calculator with different prices without re-entering dosage data or particulars of the different strengths and/or formulations of each drug.
Price proposal or Price response	Responsible persons are asked for their price responses once particulars relating to data source and sample dosage data have been settled. A price proposal, or price response, constitutes a formal offer in the sense that should a responsible person's proposed prices be the benchmark price for that product, the drug will need to be available at those prices for the various strengths.
Projected dosage data	Data providers often make adjustments to raw sample data to reflect demographic and other prescriber attributes, and factor up these data to estimated national levels. Projected and unprojected dosage data are entered in the WAMTC calculator. At an early stage in the calculations, the projected data are scaled back to match the actual sample dosage observations for each drug.
TGP	Therapeutic group premium. This is a premium charged by a manufacturer above the benchmark price of a medicine in one of the six therapeutic groups under the therapeutic group premium policy and is paid by the patient.

Therapeutic Group	Based on the therapeutic grouping policy introduced in the 1997-98 budget, a therapeutic group is a narrowly defined therapeutic sub-group where the drugs concerned are of similar safety, efficacy and health outcomes, and interchangeable on an individual patient level. The Australian Government subsidises drugs within a therapeutic group to the level of the lowest priced drug in the group, with pricing based on WAMTC methodology. Suppliers of other drugs in the therapeutic group are able to set prices above the price of the lowest priced drug with the patient paying the TGP which is the price difference between the lowest priced drug and the drug prescribed. There are currently six therapeutic groups: angiotensin converting enzyme (ACE) inhibitors; angiotensin II receptor antagonists (ATRAs); dihydropyridine-derivative calcium channel blockers (CCBs); H_2-receptor antagonists (H_2RAs); the HMG Coenzyme A reductase inhibitors simvastatin and pravastatin (statins), and proton pump inhibitors (PPIs). See section 1.2 for further detail on drugs included in the therapeutic groups.
Therapeutic relativity sheets	Therapeutic relativity sheets show specific relativities and pricing comparisons between drugs within a therapeutic group. The relativities are usually based on PBAC advice but may also be historically based. These sheets form the basis of most pricing decisions of the PBPA.
Unadjusted WAMTC	The WAMTC, based on sample dosage data alone, before there is scaling to align with relativities among Medicare Australia and DUSC script numbers.
WAMTC	Weighted Average Monthly Treatment Cost is the average cost of treating a patient with the drug for one month. A form of reference pricing, the aim of WAMTC is to adjust pricing of drugs which have been accepted by the PBAC as being therapeutically similar (on a population basis) so that their cost per month's treatment per patient is the same. The WAMTC calculation and ensuing process starts by weighting dosage data for drugs in certain groups according to aggregate levels of use and multiplying by PBS dispensed prices (less brand or therapeutic group premiums) to produce estimates of costs per month per patient for each drug for comparison purposes.

1. What is WAMTC?

The Weighted Average Monthly Treatment Cost (WAMTC) methodology is a type of reference pricing applied to particular groups of Pharmaceutical Benefits Scheme (PBS) subsidised drugs. Drugs in the same formulary, which are recommended by the PBAC for listing on a cost minimisation basis i.e. two or more drugs are considered therapeutically no worse than each other in terms of safety and efficacy. These drugs are considered to provide the same or similar health outcomes and are potentially eligible to form a WAMTC group. The premise is that those drugs which are cost minimised are treated as 'equivalent' for pricing purposes, and thus should have the same monthly treatment costs per patient, exclusive of brand or therapeutic group premiums.

Reference pricing is usually based on the therapeutic relativities of drugs, from clinical trials, as presented to the Pharmaceutical Benefits Advisory Committee (PBAC) at the time of submission i.e. 20 mg of drug X was deemed equivalent to 30 mg of drug Y. Price is then generally determined and updated on this basis.

The WAMTC methodology is intended to account for different usage practices in the market place compared with the formal clinical trial situation. Using sample data on prescribing behaviours and best available data on script volumes for each drug, a weighted average daily (and thus monthly) cost of treatment per patient can be estimated.

As an example, if drug A is listed on a cost minimisation basis versus drug B with 45 mg = 60 mg, but as used in clinical practice the average daily doses are 47 mg and 59 mg then the price for drug A should be lower and for drug B higher than based on the 45 mg = 60 mg comparison.

These differences could be due to one drug being perceived by prescribers as often needing a higher/lower dose, or due to the way the drug is promoted (eg to specialists), or the drug being used at a higher dose as it is the latest entrant and is reserved for resistant patients etc.

Like all drugs on the PBS, the prices of those drugs that form a WAMTC group are reviewed annually. Put simply, each WAMTC review involves a comparative analysis over the latest available four quarters of the estimated monthly usage and therefore cost per patient of a group of drugs.

Current drug costs are weighted by a sample of the prescribed dosages for each drug, adjusted to reflect the relativities at different strengths or formulations of Medicare Australia data and under co-payment prescription numbers over the same period. As part of the review process responsible persons are asked to submit price proposals based on the evidence of the WAMTCs for the current situation, and the estimated monthly usage cost per patient is then recalculated to take into account those price proposals. The result is that the Australian Government accepts the drug with the lowest 95% upper confidence bound for its WAMTC as the benchmark drug, and the price of the remaining drugs in the group must be such that their WAMTCs are not significantly different from that of the benchmark drug.

Following a review of the previous WAMTC methodology by Ernst & Young and ensuing negotiations with industry, a new WAMTC methodology using an approximation to the WAMTC variance that averted the complications of bootstrapping was outlined to industry in October 2003 and a WAMTC calculator distributed to automate calculations. For background on the review of the WAMTC methodology by Ernst & Young, and differences between the prior methodology and the reinstated processes see ***Attachment A***.

Refer to ***Attachment B*** for changes in WAMTC reviews since reintroduction in January 2004 including significant precedents and the impact of PBS reforms.

Refer to ***Attachment C*** for adjustments, exemptions and exclusions and ***Attachment D*** for frequently asked questions.

1.1 How a WAMTC group is formed

In theory, any group of drugs (two or more) that have been listed on the basis that they provide the same or similar health outcomes (the same or similar effectiveness and safety and listed on a cost minimisation basis) could be considered for inclusion in a WAMTC group provided they are in the same formulary.

Drugs that are listed on a cost minimisation basis usually have a dosage relativity advised by the PBAC. This dosage relativity is used to establish and to review pricing. Where there are several drugs all accepted as being similar to one another, the stated dosage relativities could be used in pricing reviews, but these relativities are rigid and there is no account of different uses in the market compared with that in the clinical trials. In these situations, it may be more appropriate to use the WAMTC methodology.

The process is that the Pharmaceutical Benefits Pricing Authority (PBPA) decides if a WAMTC group should be formed. It would be usual to seek PBAC agreement that the drugs are suitable for such a grouping (if the PBAC has not already advised this) and in the case of F2 drugs, there must be interchangeability at the individual patient level (these drugs must form a therapeutic group). It would also be possible for a drug's responsible person to suggest to the PBPA that the WAMTC methodology should be applied to a group of drugs (two or more) if it was seen that this would be appropriate for pricing review.

Therapeutic groups are designated by the Minister and are automatically subjected to the WAMTC methodology except where exemptions apply.

Where the PBPA proposes the formation of a new WAMTC group or changes to existing groups, affected responsible persons will be given sufficient notice and a formal opportunity to provide comment on the proposal.

The drug groups to which the WAMTC methodology applies can fall into two categories: therapeutic group drugs and non-therapeutic-group drugs.

1.2 Therapeutic Group drugs

- Same mode of action (generally interchangeable on individual basis)
- Similar safety and efficacy (same or non-inferior health benefits/outcomes)

Drugs in therapeutic groups are chemical entities with the same mode of action in the same pharmacological group, accepted on a cost minimisation basis and where the drugs are considered similar on an individual patient basis. The WAMTC methodology applies to all therapeutic groups.

The PBS Reform initiative introduced in August 2007 has resulted in all drugs being in either the F1 or F2 formulary (http://www.health.gov.au/pbsreform).

Reference pricing will continue to apply between drugs that are linked within reference pricing groups on F1 and within the Therapeutic Groups and across different brands of the same medicine listed on F2.

F2 drugs must be in a therapeutic group for reference pricing, including application of WAMTC, to occur.

At present there are six therapeutic groups:

- Angiotensin II Receptor Antagonists (candesartan, eprosartan, irbesartan, olmesartan, telmisartan, valsartan)
- Angiotensin Converting Enzyme (ACE) Inhibitors (captopril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolopril)
- Dihydropyridine-derivative calcium channel blockers – CCBs (dihydropyridines) (amlodipine, felodipine, lercanidipine, nifedipine)
- H_2-receptor antagonists (cimetidine, ranitidine, nizatidine, famotidine)
- HMG Coenzyme A reductase inhibitors (statins) (pravastatin, simvastatin)
- Proton Pump Inhibitors – (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole)

Diltiazem, which was part of the CCBs WAMTC group, but not the therapeutic group of calcium channel blockers, has ceased to be reference priced with other drugs in that therapeutic group.

1.3 Non-therapeutic group WAMTC group drugs

- Usually, but not necessarily have the same mode of action (may or may not be interchangeable on an individual basis)
- Similar safety and efficacy (delivering the same or non-inferior health benefits/outcomes)

Non-therapeutic groups of drugs are formed in the F1 formulary where the mode of action is not necessarily the same (interchangeable) but where the drugs have been listed on a

cost-minimisation basis as providing the same or similar health outcomes on at least a population basis. In some cases it may be that the group could form a therapeutic group but has not been so designated.

Prior to 1 August 2007 there was a non-therapeutic group of drugs subject to WAMTC review, the selective serotonin reuptake inhibitors (SSRIs) plus WAMTC group. From 1 August 2007 most of the drugs in the SSRIs-plus group were allocated to F2 and one drug in the group, reboxetine, was allocated to F1 but as the members were not allocated to a therapeutic group they are no longer subject to WAMTC review.

Currently there are no non-therapeutic group WAMTC groups.

Drugs or particular strengths or formulations which are not included in a WAMTC review but are linked through therapeutic relativities to a drug/s that are in a WAMTC group will be affected by the results of a WAMTC review and their prices adjusted according to the therapeutic relativity or the principles that apply to pricing of combination products or double strengths.

Likewise, a change in the price of a drug not included in a WAMTC review could affect and possibly trigger a WAMTC review, where it is linked through relativities to a drug that is included in either an F1 or F2 WAMTC group.

2. Steps in the process of a WAMTC review

The major steps in conducting a WAMTC review are as follows:

- determine the dosage data source to be used (unless the review is a competitive dosage data selection cycle, the source has already been determined by an assessment of earlier presented data);
- run the WAMTC calculator with current prices;
- invite price proposals, applying default provisions where no response is received;
- invite comment on any submissions received;
- undertake review and establish both benchmark drug and the lowest prices at which each formulation and/or strength of every drug in the group will be offered following the review;
- notify responsible persons of the choices that remain available to them, and a default provision, and ask them to indicate what they wish to do;
- process price changes in order for them to take effect on the due date(s).

As the time taken for some of these steps will vary according to the extent to which responsible persons differ in approach and opinion, the length of time required to finish a review will not always be the same, and the timeframes given below are necessarily indicative only. Responsible persons' interests are upheld by:

- a guaranteed ten working days in which to submit sample dosage data or to respond to the invitation to submit price proposals; and
- the opportunity to comment on submissions that may affect how their drug is assessed.

The PBPA Secretariat will work in shorter timeframes where required to meet unanticipated events or the stringency of deadlines. Communications are ordinarily by e-mail to give responsible persons as much working time as possible to prepare their responses.

The purpose of a review is to establish a realignment of prices based on changed prescribing patterns and responsible persons' price responses. As the Australian Government's policy requires reimbursement at the lowest available price where no differences in health outcomes have been established before the PBAC, there are few restrictions on which drugs are eligible to be the benchmark drug:

- drugs with fewer than 65 prescriptions in the sample dosage data are excluded from being the benchmark because that is insufficient to draw conclusions about differences with the precision desired;

- any drug with at least 65 prescriptions may be the benchmark drug for the group, if it has the lowest cost to the Australian Government.

2.1 Regular cycle of WAMTC reviews

Each WAMTC group is reviewed annually in accordance with the normal annual cycle of reviews of all ATC drug groups by the PBPA:

WAMTC Group	**Drugs in WAMTC Group**	**ATC Group**	**Items currently excluded**	**Scheduled Review† (to coincide with PBPA ATC group review)**
H_2-receptor antagonists (H_2RAs)	cimetidine, ranitidine, nizatidine, famotidine	A02		Apr
Calcium channel blockers (CCBs)	amlodipine, felodipine, lercanidipine, nifedipine,	C08	diltiazem*	Apr
Angiotensin converting enzyme (ACE) inhibitors	captopril, enalapril, fosinopril, lisinopril, perindopril, quinapril, ramipril, trandolapril	C09	captopril oral solution	Aug
HMG Coenzyme A reductase inhibitors (Statins)	pravastatin, simvastatin	C10	atorvastatin** fluvastatin***	Aug
Angiotensin II receptor antagonists (ATRAs)	candesartan, eprosartan, irbesartan, olmesartan**** telmisartan valsartan*****	C09		Dec
Proton pump inhibitors (PPIs)	esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole	A02	esomeprazole tablet 40mg	Dec

†This is the date the PBPA considers the review results. Secretariat commences reviews several weeks prior to a PBPA meeting.

* diltiazem was removed from the CCB WAMTC group as it is not interchangeable at the level of individual patients with the CCBs.

**atorvastatin was included in statin WAMTC reviews until July 2005. It is currently not reviewed with simvastatin or pravastatin, being in a different formulary.

***fluvastatin was previously linked to simvastatin for pricing purposes, until PBS Reform was implemented.

****olmesartan is to become an active member of the ATRA WAMTC group with its first review commencing December 2009.

*****valsartan is to become an active member of the ATRA WAMTC group with its first review commencing December 2010.

The following steps outline the process for a regular annual review. For a flowchart of the timelines see ***Attachment E***.

Please note: the PBPA Secretariat will endeavour to always adhere to the guidelines below. Where circumstances require the review to be conducted in a shorter timeframe, the responsible persons will always be given 10 working days at each stage they are required to respond with data or price proposals/responses. Responsible persons will be formally notified at the commencement of a review, and kept informed of the timeframes for each stage of the review.

Steps in regular annual WAMTC review process

1a Competitive process for selecting dosage data source, or request from responsible person to change dosage data source – generally 14 weeks before PBPA meeting

- For annual reviews, the same dosage data source will be maintained for a minimum of three years, unless a responsible person can show grounds to justify a change. *See **Section 3.1** for further information on data sources.*

- The next set of competitive processes for selecting data sources for particular WAMTC groups will start in December 2010 i.e. responsible persons of drugs in current groups will be invited to submit data from any eligible data provider.

- If data come in from more than one source, the PBPA Secretariat will circulate the options to each responsible person in the group as soon as possible and invite comment on which data source is preferred for the review. Note that responsible persons' comments may be circulated to the others in the WAMTC group, or other affected parties, and provided. The Secretariat will use the selection criteria in ***Attachment F*** to choose the final data source.

- If only one data source is proposed in the competitive process, that will become the data source for the group.

- If no data source is proposed in a competitive process, or where no updated data is provided by responsible persons for an established data source, the Secretariat will obtain and use BEACH data or, dosage data from another provider as required to meet WAMTC guidelines.

- The selected data source during a competitive process will then be in force for all ad-hoc and annual reviews for the group for 3 years.

- A responsible person may apply to change the dosage data competition at the end of a three-year cycle or during the three-year cycle if the responsible person can show grounds to justify a change.

- Provided that the intention to change the data source is notified at least 14 weeks before the PBPA meeting along with supporting evidence, any data source and

annotated supporting raw data will be circulated as soon as possible to the WAMTC group's other responsible persons for comment.

- Acceptance or not of a request to change the data source will made by the PBPA Secretariat based on comments received from responsible persons and the criteria outlined in ***Attachment F***. Justification for this decision will be provided to responsible persons.

- The data source (if more than one is supplied) will be determined on the basis of comments received and the Department's own assessment, making use of the data selection criteria set out in ***Attachment F***.

1b Responsible person notification and request for dosage data – generally 10 weeks before PBPA meeting

- The PBPA Secretariat sends letters to responsible persons (usually via email) notifying them of the review.

- Included are the most recent available four quarters of Medicare Australia data on prescription numbers and DUSC data on under co-payment script numbers (where under co-payment data are relevant), with appropriate notes.

- The latest available under co-payment data (which generally become available three months following the end of a particular quarter) will in practice determine the twelve-month period of data to be used in the review. It may overlap with the period used for the previous annual review.

- Responsible persons are invited to submit dosage data on all drugs in the WAMTC group for the specified twelve-month period within ten working days. The pooled usage data on all brands of a drug, or all items where bioequivalence or therapeutic equivalence is indicated in the schedule, are used in the calculator. For annual reviews, the same dosage data source will be maintained for a minimum three year period unless a responsible person can show grounds to justify a change. *See Step 1a* above.

2. Dosage data submissions – generally 8 weeks before PBPA meeting

- The cut-off for receiving dosage data is 8 weeks prior to the PBPA meeting.

- The PBPA Secretariat will obtain BEACH dosage data or, dosage data from another provider if required, as a backup in the event that responsible persons do not submit any updated dosage data.

3. Raw data management and WAMTC calculation

- The PBPA Secretariat enters information into the WAMTC calculator using the current cost to Australian Government (ie DPMQ less any BPs or TGPs or SPCs),

taken from the latest PBS Schedule. Co-payments are ignored for these and subsequent calculations in the WAMTC review process. See ***Attachment G*** for what goes into the calculator.

- The WAMTC calculator is run to determine the current benchmark drug (drugs with current TGPs or with dosage samples with <65 observations are not eligible to be the benchmark in this initial calculation).

- The WAMTC calculator runs a global test (chi-square test) to determine whether there is any statistical difference between the WAMTCs of the drugs in the group. If a difference is found, the pair-wise tests (z-tests) between the benchmark drug and each other drug in the group are used to determine the extent to which each drug would have to reduce its prices in order to match, exactly, the WAMTC of the benchmark drug (the point estimate). For those drugs not statistically different from the benchmark drug, no price reductions are indicated.

- A drug with fewer than 65 scripts in the sample dosage data is still used in the WAMTC calculations. It cannot be the benchmark drug, and will be removed from the calculation if that appears to be the case. However, it will be required to take a price reduction if it has a WAMTC statistically significantly higher than that of the benchmark drug.

- Where the global test indicates that there is no statistically significant difference between the WAMTCs of the drugs in the group, no price reductions will be indicated. However, responsible persons will always have the opportunity at a regular annual WAMTC review to submit a price proposal (see below). The proposed prices may result in changes to the benchmark drug and/or WAMTC and further action may be required by other responsible persons.

- Responsible persons should note that a different drug may be the benchmark once price responses have been received. A drug with a previous TGP may end up as the benchmark drug, if it has the lowest cost to the Australian Government.

4. Request for price proposals – generally 6 weeks before PBPA meeting

- The PBPA Secretariat sends letters to responsible persons requesting price proposals

- The letters include:
  - the WAMTC pre-calculation file and dosage data, raw and projected, and any notes to facilitate an understanding of what has been done. See ***Section 4.1*** for detail on the pre-calculation file and interpreting the results
  - information on the current benchmark drug and across-the-board price reductions needed if WAMTCs remain statistically significantly higher than that of the current benchmark drug; and
  - a customised price proposal template. See ***Attachment H*** for a copy of the template**.**

- Price proposals are for the cost to the Australian Government (ie cost to the PBS). Responsible persons cannot request TGPs or BPs at this time as the benchmark drug for the review is not finalised until price proposals are received, and the benchmark price for each drug is likewise not yet determined.

- If no price proposal is received, the default price will be the current DPMQ less any amount for a BP or TGP (ie the cost to the Australian Government)

- A proposal to increase a price must be accompanied by a PB 11(b) form. The PBPA will consider factors such as cost of manufacture, as per normal procedures in considering a price increase request (see the *PBPA Policy, Procedures and Methods Manual* for more detail).

- A PB 11(b) form is required when responsible persons are seeking an increase in the cost to the PBS. This may not be an increase in price to pharmacist for those drugs with a previous TGP or BP or SPC, but an increase in the cost borne by the Australian Government. That is, a PB 11(b) form is required when the price in column 3 'Price response' of the price proposal template (***Attachment H***), is greater than the price in column 4 'Default entry if no response is received'.

- Where a price increase is sought, or some other decision is required from the PBPA in relation to a submission, a contingent price proposal may be made rather than there being an automatic fall-back to the previous prices. *See* ***Attachment H***. If no contingent price is proposed in this circumstance, and the PBPA rejects the submission, the default price will be the same as for a nil response, current DPMQ less any amount for a BP or TGP or SPC. Should the PBPA accept a partial amount of a requested price increase only, the responsible person will be notified.

- Submissions potentially affecting the interests of other responsible persons (and sometimes others such as sample dosage data providers) are circulated for comment. If they wish some matters to remain commercial-in-confidence, the responsible person may provide a version of their full submission that is suitable for circulation.

5. Price proposals deadline – generally 4 weeks before PBPA meeting

- Where no response is received the default price that applies is the DPMQ less any previous amount for BPs or TGPs or SPCs.

- Responsible persons not wanting their drug to be the benchmark should take care to submit an appropriate price response as application of the default provision may resulting an outcome that they wish to avoid.

6. WAMTC calculation using price responses

- The PBPA Secretariat re-runs the WAMTC calculator with the price proposals of the various responsible persons. (Note: if no price response is received from a

responsible person, the previous BP or TGP or SPC will be subtracted from the previous DPMQ and will be used as the basis for the calculation).

- The lowest proposed price for each strength and/or formulation of each drug is used in this calculation.

- Provided that its sample dosage data have at least 65 observations, the benchmark drug can now be determined as that with the lowest 95% upper confidence bound.

- The final benchmark drug and its WAMTC can only be determined after price proposals are received from responsible persons. No TGPs or BPs or SPCs exist at this stage.

- No drug is exempt from becoming the benchmark at this stage based on a previous application of a TGP, or BP or SPC.

7. PBPA agenda paper prepared – 2 weeks before PBPA meeting

- The PBPA Secretariat prepares an agenda item for the PBPA meeting to facilitate the WAMTC review. Comments received from responsible persons and possibly other parties are included in this material

- Key facts, such as the benchmark drug and WAMTC, and the benchmark price for each formulation and/or strength of every drug, are determined by the PBPA. Other decisions necessary to finalise a WAMTC review, such as consideration of requests for adjustment or exemption or price increases, are also made.

8. Notify responsible persons of PBPA outcome and invite final price confirmation – post PBPA meeting

- The PBPA Secretariat sends letters to responsible persons informing them of the PBPA assessment of the benchmark drug and prices and invites responsible persons to advise of moves to the benchmark price or the levels of premiums required i.e. BPs or TGPs, where appropriate.

- A template for price responses, outlining all the available options with annotations, will be included in each notification to individual responsible persons. The required WAMTC for each drug is specified at this stage, with point-to-point reductions necessary where a WAMTC was found to be statistically greater than that of the benchmark drug.

- Unsuccessful proposals of price reductions by responsible persons not supplying the full range of strengths and/or formulations will be set aside in assessing what reductions are required to achieve the benchmark WAMTC.

- Multiple responsible persons of a drug whose WAMTC is greater than that of the benchmark drug will face across-the-board percentage reductions as that avoids the prospect of further downward ratcheting of prices.

- Where their drug's WAMTC is statistically greater than that of the benchmark drug, sole suppliers of all strengths of a drug may apply another mix of price reductions to achieve the necessary point-to-point WAMTC reduction. This will involve for certain strengths a reduction by more than the percentage required across-the-board, if there is a desire to maintain current prices or limit reductions at some strengths. Such proposals will need to comply with the PBPA's guidelines for pricing at different strengths.

- Responsible persons should be aware that the lowest price at each strength and/or formulation of every drug arising from price proposals must be available, and must be prepared to shoulder the responsibility of guarantee of supply as proposers if no-one else does. Other responsible persons have the option of applying a BP of whatever size they regard as appropriate.

- In a therapeutic group, sole suppliers of a formulation or strength of a drug whose WAMTC is statistically equal to that of the benchmark drug may apply a TGP of whatever size they regard as appropriate. If instead a point-to-point reduction in a drug's WAMTC is required, a sole supplier can achieve this partially or wholly through the application of one or more TGPs.

9. Price changes for PBS Schedule – cut-off approximately 4 weeks after PBPA meting

- Responsible persons will have a deadline for final price responses, within the specified constraints and applying after the PBPA has conducted its review, no earlier than ten working days from notification. A default provision will be set out in the event that no advice is received.

- Approximately one month after the PBPA meeting, the PBPA Secretariat finalises new prices for the next release of a PBS schedule where prices may change

2.2 Ad hoc WAMTC reviews

An ad hoc review of a WAMTC group is triggered by a price reduction to any brand of a drug in WAMTC group including through the entry of a new responsible person.

The PBPA has determined that for an ad hoc review the same dosage data source will be used as at the preceding annual review. For a flowchart of the timelines for an ad hoc WAMTC review see ***Attachment I***.

Please note: if an offer of a price reduction is received after the 10-week cut-off, the brands of the same chemical will be subject to a price reduction or a Brand Premium can apply, while an ad hoc review for the other drugs in the WAMTC group will take place in time for the next available PBPA meeting, if the global test shows this is necessary.

Steps in an ad hoc WAMTC review process

1. Price reduction offered by a responsible person – at least 10 weeks before PBPA meeting

- An ad hoc review is triggered when a responsible person of a drug in a WAMTC group offers a price reduction.

- The responsible person requesting the price reduction should submit dosage data at that time, from the same source as at the preceding annual review (unless a change has been effected in the interim through responsible person action.

- If that responsible person cannot access the relevant data, other responsible persons will be notified and given the opportunity to submit the data (an extra fortnight will need to be allowed in this event), and the PBPA Secretariat will simultaneously obtain BEACH data or, dosage data from another provider if required in the event that no data are submitted by responsible persons.

2. Dosage data submissions – generally 8 weeks before PBPA meeting

- The cut-off for receiving updated dosage data is 8 weeks prior to PBPA meeting.

- The PBPA Secretariat will obtain BEACH dosage data or, dosage data from another provider if required as a backup in the event that responsible persons do not submit updated dosage data.

3. Raw data management and WAMTC calculation

- Once dosage data have been received and cleaned, the calculator is run and the global test for equality of all WAMTCs determines whether a full ad hoc review is necessary.

- The PBPA Secretariat enters information into the WAMTC calculator using the current cost to the Australian Government (ie DPMQ less any BPs or TGPs or SPCs), taken from the latest PBS Schedule. Co-payments are ignored for these and subsequent calculations in the WAMTC review process. See ***Attachment G*** for what goes into the calculator.

- The WAMTC calculator is run to determine the current benchmark drug (drugs with current TGPs or with dosage samples with <65 observations are not eligible to be the benchmark in this initial calculation).

- The WAMTC calculator runs a global test (chi-square test) to determine whether there is any statistical difference between the WAMTCs of the drugs in the group. If all WAMTCs are statistically equal, other responsible persons of the drug for which reductions have been proposed are asked whether they wish to match that price or to impose a brand premium. Only in the event that data have been sought from the remaining responsible persons will it be necessary to tell them that an ad

hoc review is not required.

- If not all WAMTCs are statistically equal, a full ad hoc review is triggered. The pair-wise tests (z-tests) between the benchmark drug and each other drug in the group is used to determine the extent to which each drug would have to reduce its prices in order to match, exactly, the WAMTC of the benchmark drug (the point estimate). For those drugs not statistically different to the benchmark drug, no price reductions are indicated.

- A drug with fewer than 65 scripts in the sample dosage data is still used in the WAMTC calculations. It cannot be the benchmark drug, and will be removed from the calculation if that appears to be the case. However, it will be required to take a price reduction if it has a WAMTC statistically significantly higher than that of the benchmark drug.

- Responsible persons should note that a different drug may be the benchmark once the price responses have been received. A drug with a previous TGP may end up a benchmark drug, if it has the lowest cost to the Australian Government.

4. Request for pricing proposals – generally 6 weeks before PBPA meeting

- Where the global test indicated that not all WAMTCs are statistically equal, the PBPA Secretariat sends letters to responsible persons requesting price proposals.

- The letters include:
  - the WAMTC pre-calculation file and dosage data, raw and projected, and any notes to facilitate what has been done. See ***Section 4.1*** for detail on the pre-calculation file and interpreting the results;
  - information on the current benchmark drug and across-the-board price reductions needed if WAMTCs remain statistically significantly higher than that of the current benchmark drug; and
  - a customised price proposal template**.** See *Attachment H.*

- Price proposals are for the cost to the Australian Government. Responsible persons cannot request TGPs or BPs at this time as the benchmark drug for the review is not finalised until price proposals are received, and the benchmark price for each drug is likewise not yet determined.

- If no price proposal is received, the default price will be the current DPMQ less any amount for a BP or TGP (i.e. the cost to the Australian Government).

- A proposal to increase a price must be accompanied by a PB 11(b) form. The PBPA will consider factors such as cost of manufacture, as per normal procedures in considering a price increase request (see the *PBPA Policy, Procedures and Methods Manual* for more detail).

- A PB 11(b) form is required when responsible persons are seeking an increase in

the cost to the PBS. This may not be an increase in price to pharmacist for those drugs with a previous TGP or BP or SPC, but an increase in the cost borne by the Australian Government. That is, a PB 11(b) form is required when the price in column 3 'Price response' of the price proposal template (***Attachment H***), is greater than the price in column 4 'Default entry if no response is received'.

- Where a price increase is sought, or some other decision is required from the PBPA in relation to a submission, a contingent price proposal may be made rather than there being an automatic fall-back to the previous prices. See ***Attachment H***. If no contingent price is proposed in this circumstance, and the PBPA rejects the submission, the default price will be the same as for a nil response, current DPMQ less any amount for a BP or TGP or SPC. Should the PBPA accept a partial amount of a requested price increase only, the responsible person will be notified.

- Submissions potentially affecting the interests of other responsible persons (and sometimes others such as sample dosage data providers) are circulated for comment. If they wish some matters to remain commercial-in-confidence, responsible persons may provide a version of their full submission that is suitable for circulation.

5. Price proposals deadline – generally 4 weeks before PBPA meeting

- Where no response is received, the default price that applies is the DPMQ less any previous amount for BPs or TGPs or SPCs.

- Responsible persons not wanting their drug to be the benchmark should take care to submit an appropriate price response as application of the default provision may result in an outcome that they wish to avoid.

6. WAMTC calculation using price responses

- The PBPA Secretariat re-runs the WAMTC calculator with the price proposals (Note: if no price response is received from a responsible person, the previous BP or TGP or SPC will be subtracted from the previous DPMQ and will be used as the basis for the calculation).

- The lowest proposed price for each formulation of each drug is used in this calculation.

- Provided that its sample dosage data has at least 65 observations, the benchmark drug can now be determined as that with the lowest 95% upper confidence bound.

- The <u>final</u> benchmark drug and its WAMTC can only be determined at this stage based on a previous application of a TGP, or BP, or SPC.

7. PBPA agenda paper prepared – 2 weeks before PBPA meeting

- The PBPA Secretariat prepares an agenda item for the PBPA meeting to facilitate

the WAMTC review. Comments received from responsible persons and possibly other parties are included in this material.

- Key facts, such as the benchmark drug and WAMTC, and the benchmark price for each formulation and/or strength of every drug, are determined by the PBPA. Other decisions necessary to finalise a WAMTC review, such as consideration of requests for adjustment or exemption or price increases, are also made.

8. Notify responsible persons of PBPA outcome and invite final price confirmation post PBPA meeting

- The PBPA Secretariat sends letters to responsible persons informing them of the PBPA assessment of the benchmark drug and prices and invites responsible persons to advise of moves to the benchmark price or the levels of premiums required i.e. BPs or TGPs, where appropriate.

- A template for price responses, outlining all the available options with annotation will be included in each notification to individual responsible persons. The required WAMTC for each drug is specified at this stage, with point-to-point reductions necessary where a WAMTC was found to be statistically greater than that of the benchmark drug.

- Unsuccessful proposals of price reductions by responsible persons not supplying the full range of strengths and/or formulations will be set aside in assessing what reductions are required to achieve the benchmark WAMTC.

- Multiple responsible persons of a drug whose WAMTC is greater than that of the benchmark drug will face across-the-board percentage reductions as that avoids the prospect of further downward ratcheting of prices.

- Where their drug's WAMTC is statistically greater than that of the benchmark drug, sole suppliers of all strengths of a drug may apply another mix of price reductions to achieve the necessary point-to-point WAMTC reduction. This will involve for certain strengths a reduction by more than the percentage required across-the-board, if there is a desire to maintain current prices or limit reductions of some strengths. Such proposals will need to comply with the PBPA's guidelines for pricing at different strengths.

- Responsible persons should be aware that the lowest price at each strength and/or formulation of every drug arising from price proposals must be available, and must be prepared to shoulder the responsibility as proposers if no-one else does. Other responsible persons have the option of applying a BP of whatever size they regard appropriate.

- In a therapeutic group, sole suppliers of a formulation or strength of a drug whose WAMTC is statistically equal to that of the benchmark drug may apply a TGP of whatever size they regard as appropriate. If instead a point-to-point reduction in a

drug's WAMTC is required, a sole supplier can achieve this partially or wholly through the application of one or more TGPs.

9. Price changes for PBS Schedule– cut-off approximately 4 weeks after PBPA meeting

- Responsible persons will have a deadline for final price responses, within the specified constraints and applying after the PBPA has conducted its review, no earlier than ten working days from notification. A default provision will be set out in the event that no advice is received.

- Approximately one month after the PBPA meeting, the PBPA Secretariat finalises the new prices for the next release of the PBS Schedule where prices may change.

3. Data

- For regular annual reviews, the same dosage data source will normally be maintained for a minimum three years after responsible persons have had an unrestricted opportunity to provide data from what they regard as the most appropriate source.
- Where responsible persons wish to change the dosage data source within the three-year cycle, they will need to establish that the current source has adjusted and unadjusted WAMTCs quite some distance apart (in terms of estimated adjusted WAMTC standard deviations) for a majority of the drugs in the group that have multiple strengths and/or formulations. The proposed replacement will need to have these estimated WAMTCs a smaller distance apart for a majority of the drugs that are more than two standard deviations apart for the default source and/or formulations. As a guide, the criteria outlined in ***Attachment F*** will need to be addressed by the responsible person.
- For an ad hoc WAMTC review, the responsible person initiating the review, or another responsible person, should supply the latest four quarters' data from the same source as used in the preceding annual review. If no data are forthcoming, the PBPA Secretariat will arrange for BEACH data or, dosage data from another provider if required to be available.
- Any new drugs added to a WAMTC group are not included in calculations until there are four continuous quarters' data available.
- Any new strength of an existing drug is included in the data as soon as particulars of its prescribing become available unless the PBPA determines otherwise.
- The PBPA Secretariat will determine the dosage data source and which observations are used in the calculator after consultation with affected parties, where necessary. The PBPA Secretariat will notify responsible persons of the detailed reasons for the selection of the chosen dosage data source.
- Data sources with high degrees of clustering may be excluded from eligibility by the PBPA Secretariat before the start of the review, and remain so until their sampling procedures comply with what allows the WAMTC variance approximation in the calculator to apply.

3.1 Dosage data sources

The following table outlines when the next opportunity for competitive provision of the dosage data source will arise, and, in brackets where relevant, the source to be used for any ad hoc WAMTC review before then.

WAMTC Group	Data selection time (and current source)
Angiotensin converting enzyme (ACE) inhibitors	August 2011 (BEACH)
HMG Coenzyme A reductase inhibitors (Statins)	August 2011 (BEACH)
Angiotensin II receptor antagonists (ATRAs)	December 2011 (GPRN)
Calcium channel blockers (CCBs)	April 2011 (BEACH)
H_2- receptor antagonists (H_2RAs)	April 2011 (AMI)
Proton pump inhibitors (PPIs)	December 2010 (BEACH)

Dosage particulars are available as sample information for prescribing by GPs from a number of commercial sources including:

- long-standing Australian Medical Index (AMI) data from IMS Health Australia;
- Bettering the Evaluation and Care of Health (BEACH) data from the General Practice Statistics and Classification Unit of the AIHW and University of Sydney that has been built up since 1998;
- General Practice Research Network (GPRN) data collected since 2000 from a panel of GPs prescribing electronically through the Medical Director software of the Health Communication Network (HCN).

Responsible persons are asked to provide updated dosage data at each regular or ad hoc review. Where no responsible person provides data, the PBPA Secretariat will obtain BEACH data or, dosage data from another provider if required (this is irrespective of what the previous data source may have been).

Dosage data used in WAMTC reviews are derived from samples of varying size and composition, available either quarterly or over other specified periods. Twelve months' continuous data are required for the WAMTC calculation. The twelve-month period for which data must be obtained is specified to responsible persons and is based on the latest available quarterly DUSC under co-payment data[1]. Where the WAMTC group is not affected by under co-payment scripts, DUSC data are not required and the latest available quarter of Medicare Australia data will be used as the cut-off.

There are standard techniques for demographic adjustment so that what is actually known about the population profile of doctors and patients is reflected in the adjusted prescribing data. The sum of Medicare Australia script numbers and DUSC under co-payment estimates is used to realign relativities between different formulations and/or strengths of

[1] The PBPA Secretariat will use the latest available four quarters' data. From time to time overlapping data periods may need to be used for consecutive annual reviews if non-overlapping data are not available at commencement of a review.

different drugs so that the WAMTC calculation reflects overall prescribing behaviour.

Techniques for minimising the levels of unusable responses are applied by the PBPA Secretariat in 'cleaning' the data. Incomplete data entries are ignored from the sample, and the plausibility of unusual dosages checked by a medical or pharmaceutical advisor.

Provided that the overall sampling frames have no major flaws when it comes to their ability to pick out a representative snapshot of prescribing activity, the WAMTC point estimates from different sources should be quite close together once sample numbers are reasonably big. In such circumstances, the larger the available sample size, the better should the accuracy and precision of estimates become – in particular, their variance ought to become smaller.

The criteria for selecting a data source in circumstances where more than one has been put forward by responsible persons can be found at ***Attachment F***.

3.2 How to submit dosage data

The raw data, as sent from the data provider, are not in a format ready to be entered into the calculator. A responsible person submitting data should attempt to 'clean' the data by ignoring observations that are:

- incomplete (eg do not specify strength, or dose, or frequency);
- improbable (eg splitting capsules into half doses); or
- incorrect (eg refers to a strength that is not listed on the PBS or prescribes an injection when that form of the drug is not listed on the PBS).

Structuring the data to be used in a form suitable for the creation of a pivot table will enable easy summation of the observations for entry into the calculator.

Dosage data should be sent in such a format as an e-mail attachment that also includes the raw data from which it was derived, the clean data and resulting pivot table (where possible) and notes about any issues encountered in processing and how these were dealt with.

The table below sets out some manufactured dosage data, as it would be entered into the calculator.

Tablet/capsule strength (in mg)	No. of tablets/capsules per dose	No. of doses taken per day	Projected	Unprojected
10	0.5	1	4886	8
10	1	1	344712	629
10	1	2	512	1
10	2	1	665	1
20	0.5	1	8627	15
20	1	1	1328875	2607
20	1.5	1	1463	3
40	0.5	1	9773	18

40	1	1	1864286	3643
40	1	2	1104	2
40	1.5	1	997	2
40	2	1	46642	81

Please provide data in such a format that the information you are proposing be used in the calculator is easily accessible (such as in the above table format or a pivot table). See ***Attachment G*** for further information on what goes into the calculator.

A blank version of the WAMTC calculator is available from the PBPA Secretariat on request and has been placed on the Internet (http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-pricing-wamtc). Responsible persons should have all the information required for starting up a fresh calculator with particular dosage data sets, in order to assess the preference for a particular data source using the criteria outlined in ***Attachment F***. Medicare Australia and DUSC script numbers will be sent to responsible persons at notification of a WAMTC review.

3.3 Handling of deleted item codes

During the four consecutive quarters over which prescribing data are obtained for a WAMTC review, sometimes an item has been deleted.

WAMTC calculations make use of prices to the Australian Government prevailing at the time of a review and as much complete dosage data for individuals as possible from the past twelve-month period to establish whether price responses result in estimated average costs per patient being statistically the same or whether further adjustments are necessary.

If one or more items with the same strength and formulation as that of the deleted item remain on the PBS Schedule, the prescribing data for the deleted item are allocated to these remaining items. Typically the dosage data for all these items will have also been combined previously.

The second possibility is that the strength and formulation of the deleted item is no longer available on the PBS. In these circumstances, the PBPA has determined that its dosage data should be assigned, with any adjustments logically necessary, to the remaining item or items most likely to be prescribed in its place for the patients involved.

The situation first arose when the cimetidine 800mg effervescent tablet, previously available via item codes 1156W, 4976X, and 8901L, was delisted. On medical and pharmacological advice, its prescribing data were added to those for the ordinary cimetidine 800 mg tablet that remained on the PBS.

In other circumstances, if the lowest strength of a particular drug were deleted, all the dosages recorded for it might be halved and assigned to the item or items covering double that strength. Similarly if the highest strength were deleted, double the individual dosages recorded for it could be assigned to a remaining strength of half that level.

Where there are no clear-cut alternatives remaining after a delisting, the PBPA Secretariat will obtain medical advice about what is likely to happen in the case of such patients, as well as assessing suggestions and evidence that responsible persons may provide. In the absence of convincing information about where the past usage no longer possible would be likely to move, the dosage data for the deleted item might be set aside as being incapable of readily being assigned to items that remain.

3.4 Handling of drugs with the same strength and pack size, but different formulations

The degree to which prescribing information is available separately for different formulations at the same strength usually determines how entries are combined and arranged in the WAMTC calculator in such instances.

If the formulations are priced identically (perhaps for a tablet and capsule) and a sizeable portion of the prescribing data does not distinguish between these formulations, normally all available data with clear dosages for any formulation will be combined (omeprazole 20 mg tablets and capsules are one example in practice) rather than the information that is not clear about formulation being set aside as unusable. This is in line with the principle that as much as possible of the available sample data is reflected in each drug's WAMTC estimate.

Such pooling is not possible if the formulations are priced differently (for instance, with the 20mg ordinary and controlled release tablet forms of nifedipine). In such cases, prescribing information that does not specify the formulation must be set aside along with all the other dosages that are incomplete or otherwise unusable. Separate markers will have to be assigned to the different formulations (20 and 20.0001, for instance) or else the WAMTC calculator will come to a halt when it reaches what appears to be inconsistent price information.

3.5 Handling of products marked as bioequivalent or therapeutically equivalent

The PBS Schedule marks with an "a" or "b" entries where the responsible persons have submitted evidence that they have been demonstrated to be bioequivalent or therapeutically equivalent, or that justification for not needing bioequivalence or therapeutic equivalence data had been provided to and accepted by the Therapeutic Goods Administration. It would thus be expected that those brands may be interchanged without differences in clinical effect.

Prescribing data for all brands of a particular formulation and strength are always combined.

In addition, where items arising from different strength/formulation combinations are marked as bioequivalent or therapeutically equivalent (for instance, perindopril in salt form arginine at strengths 2.5mg, 5mg, and 10mg has been demonstrated as bioequivalent

to the drug presented in salt form erbumine at strengths 2mg, 4mg and 8mg respectively), prescribing data for both or all items so marked are combined (the individual dosages for 2.5 mg perindopril arginine are aggregated with those for 2 mg perindopril erbumine, and so on) as they will be priced identically.

4. The WAMTC calculator

4.1 The Pre-calculation File

The PBPA Secretariat sends a "pre-calculation" file to responsible persons when requesting price proposals. The PBPA Secretariat will have entered all relevant data for the WAMTC group into the worksheets for each of its drugs. This includes sample dosage data and Medicare Australia and DUSC script numbers as well as current prices (either as they appear in the PBS Schedule, less any BPs or TGPs or SPCs, or in the case of an ad hoc review, with one or more lower prices for the drug through which a responsible person initiated the review).

The pre-calculation file is activated by a button on the worksheet containing usage and other particulars for the final drug in the group. Several macros are run and calculations made page-by-page to give adjusted and unadjusted WAMTCs for each drug as well as estimated variances and 95% confidence intervals, and then global chi-square test and pairwise z-test results that are found on the *Summary Sheet* worksheet. Various details from this sheet will have been presented in the corresponding letter to responsible persons, along with some points of guidance for the formulation of price proposals.

Two further worksheets are filled after the calculator has been run, namely the *Adjusted WAMTC chart* and the *Unadjusted WAMTC chart* sheets. These charts plot the estimated WAMTC for each drug and its 95% confidence interval. Provided that there are at least 65 prescriptions for it in the sample dosage data, the drug with the lowest upper confidence bound in the adjusted calculations is the benchmark drug. The adjustment that is made to the sample dosage data aligns it with relativities between various strengths and/or formulations observed in aggregate Medicare Australia script numbers and estimated DUSC under co-payment data, to project total population usage and average monthly treatment cost per patient.

The pre-calculation file can be altered to assess how various changes in prices would affect the WAMTC results. Responsible persons are encouraged to save a pre-calculation version of the file separately, and work on a copied version to help them examine various scenarios out of whose analysis they are likely to formulate price proposals. Once the calculator has been run, it is not possible to get back to just the original data entered for each drug without reopening a saved version of the pre-calculation file.

Many of the entries on the *Summary Sheet* worksheet arise from formulae that are pre-entered in the pre-calculation file and populated as calculations are undertaken for each drug. Often they will change in line with an estimated WAMTC variance that decreases as

proposed prices are reduced. While interpolation of test results may be helpful for honing in on an exact price level at which a test result changes, it is always prudent to run the calculator with the selected prices to confirm that the approximation being relied upon was close enough not to upset the desired outcome. See ***Attachment J*** for tips on honing in on the crossover value for a WAMTC no longer being significantly greater than that of the benchmark drug.

Attachment G outlines how the WAMTC calculator file works. A blank version of the WAMTC calculator file is available from the PBPA Secretariat on request and can be found on the Internet at http://www.health.gov.au/internet/main/publishing.nsf/Content/health-pbs-general-pricing-wamtc

4.2 Interpreting results after price proposals have been received

Price proposals set out what each responsible person wants as the cost to the Australian Government for a particular drug. They do not involve either BPs or TGPs as these can only be determined once the benchmark drug has been determined and the lowest price at which each strength and/or formulation of every drug will be available has been established.

All drugs are eligible to be the benchmark drug unless there are fewer than 65 observations for their prescriptions in the sample dosage data. Provided that these conditions are met, the benchmark drug is identified as the one with the lowest 95% upper confidence bound (but not necessarily the lowest WAMTC).

This provides the strongest basis for detecting actual pairwise differences between drugs' WAMTCs as estimated variances are important in the z-statistic calculation arising from the difference between two normal distributions (which can reasonably be assumed from the Central Limit Theorem because of the large numbers involved).

Drugs whose WAMTC 95% confidence intervals lie entirely above that for the benchmark drug will always be found to have significantly higher WAMTCs. Other drugs whose WAMTC 95% confidence interval partially overlaps with that of the benchmark drug may also be found to fit into that category if the difference in the two WAMTC point estimates is large enough relative to each of the two estimated WAMTC variances.

There are just two possibilities for each drug other than the benchmark drug in relation to its WAMTC once price proposals have been entered into the calculator:

- either the global chi-square test or the z-test comparison with the benchmark drug's WAMTC establishes that its WAMTC is not significantly greater, in which case no further price reductions are required (and a BP or TGP of unrestricted size may be applied by a responsible person not offering the lowest price for a particular formulation or strength, or, in therapeutic groups, that is the only supplier of a

particular formulation or strength);
- the global chi-square test indicates significant differences among the WAMTCs and a drug's WAMTC is significantly greater than that of the benchmark drug, in which case a point-to-point reduction in its WAMTC will be necessary (in a therapeutic group, it may be possible to achieve this through a reduction in the cost to the Australian Government or application of one or more TGPs, or a combination of the two).

Where global test indicates no significant difference

Cell D1 on the *Summary Sheet* worksheet presents the results of a standard global chi-square test for equality of all adjusted WAMTCs which is developed on that page line-by-line in the cell blocks H24:K24 and below – in the event of a low chi-square value, there is no evidence of significant differences among the adjusted WAMTCs, and there is no basis for mandatory price reductions in that case (the z-statistics calculated in cells M24 and below will generally be small but one or more may still be significant without necessitating a price impact).

Where global test indicates significant difference

If the global statistical test indicates a significant difference in WAMTCs for drugs in the group, at least one of the pair-wise comparisons with the benchmark drug will be significantly different from zero (the null hypothesis is of two normal distributions with the same mean).

Where drugs have significantly higher WAMTCs than the benchmark drug, the overall percentage level of price reduction required in relation to them is set out in cell C5 or one immediately below it on the *Summary Sheet* worksheet. The level of price reduction required to match the WAMTC of the benchmark drug is calculated by comparing the two point estimates in question, namely by taking the gap above the benchmark drug's WAMTC point estimate as a proportion of the non-benchmark drug's WAMTC point estimate.

Price reductions

In a case where a reduction in the WAMTC is required because a difference from the benchmark drug's WAMTC has been demonstrated significant by the pairwise z-test, the *Summary Sheet* worksheet of the calculator only provides (in cell C5 or one of those immediately below) a percentage decrease across all strengths for the drug that will achieve the same WAMTC as that of the benchmark drug.

Where there are multiple suppliers of the drug in question, the same level of reduction is required across all formulations and strengths as otherwise there could be a further downwards ratcheting as a result of a lower offer yet being received for one or more formulations or strengths.

Where a price reduction is indicated for a single supplier of a drug, the specified level can

be achieved through different percentage reductions among the various strengths available, provided that these lead to appropriate ratios of prices at different strengths and the WAMTC of the benchmark drug is matched as a result.

In a therapeutic group, a reduction in a drug's WAMTC can be achieved through application or amendment of one or more TGPs, a reduction in the cost to the Australian Government or a combination of the two mechanisms available.

Note that the percentage reductions indicated in the calculator are all at dispensed prices. This translates to a slightly higher percentage reduction in cost to manufacturer.

Brand premiums

Price proposals establish the lowest price at which each formulation or strength of every drug must be offered once the outcomes of a review are implemented. All responsible persons must meet the lowest offered price or indicate that a BP will be applied.

Provided it is confident that another responsible person is likely to take up lower prices that enable a drug to be treated as though its WAMTC is not significantly different from that of the benchmark drug, a responsible person with BPs or even TGPs at some strengths or formulations in an overall multiple-supplier environment for a drug can take action so that the risk of point-to-point reductions being required for that drug is minimised.

ATTACHMENT A
BACKGROUND ON WAMTC, THE ERNST & YOUNG REVIEW, AND REINSTATING THE WAMTC METHODOLOGY

Early WAMTC

The initial use of a cost per month of treatment methodology was introduced at the time of the formation of the Pharmaceutical Benefits Pricing Authority in 1988. Scripts costing $30 or more (dispensed price) per month, and with a cheaper alternative drug already listed, were listed as 'authority required' items. The estimated cost per month was based on PBS prescription data and dispensed costs.

In 1992, a revised methodology for estimating monthly costs was proposed by industry and agreed to by all parties. This was designed to take account of actual dosage directions by prescribers. The total cost of all scripts for all strengths was divided by total period of treatment to obtain an average cost per month.

With the introduction of cost effectiveness as part of the criteria for PBS subsidy, the Pricing Authority's role shifted focus toward a pricing comparison for drugs of the same class. Initial list prices were based on relativity between drugs from clinical trials. The intention of a weighted average monthly treatment cost (WAMTC) comparison is to take account of different dosages actually used in practice. Dosages may change over time and the clinical trial setting may not have been optimal i.e. may not have reflected what would be prescribed in actual practice.

With more focus on WAMTC, the Therapeutic Group Premium (TGP) policy was introduced on 1 February 1998 (see *Appendix 1*). For a group of drugs considered clinically similar, the Australian Government subsidises to the level of the lowest priced drug. Suppliers of the other drugs are allowed to set the level of patient-paid premiums. Drugs in TGP groups were subject to WAMTC to determine pricing.

At this time, when a WAMTC review was conducted, all WAMTC point estimates had to be equal to that of the benchmark drug.

Independent review of WAMTC (2000-01)

Industry had for some time been seeking an independent review of the WAMTC methodology, and in 1999 the then Minister for Health and Aged Care agreed to a review. In 2000, after a tendering process, Ernst & Young were contracted to conduct an independent review of the WAMTC methodology.

The main issues which emerged from the Ernst & Young report were that:

- by using sample dosage data, the methodology could result in price adjustments due to

sampling error;
- as such, price reductions were almost certain despite there being no 'real' differences;
- under co-payment prescriptions were not being captured by Health Insurance Commission (HIC) (now Medicare Australia) processing data; and
- there is potential for inconsistency in dosage data supplied to the Department.

Reinstating WAMTC (2003)

A joint Medicines Australia and Pharmaceutical Benefits Branch (PBB) working group was established to address the outcomes of the Ernst & Young report. The working group agreed that the sampling error should be taken into account. Whilst the report proposed the use of bootstrapping* to account for sampling error, a different methodology was agreed on which made the calculations easier to manage and fixed all WAMTC variance estimates. Industry experts came up with a formula-based approximation technique for estimating WAMTC variances instead of bootstrapping, which leads to estimates that others cannot necessarily replicate. The benchmark drug would now be the one with the lowest 95% upper confidence bound, and not necessarily the one with the lowest WAMTC point estimate.

The working group did not decide on a preferred dosage data source. However, it was agreed that the data source must be the same for all drugs and all brands within a WAMTC group and be for a period of four consecutive quarters. The projected dosage figures (rather than unprojected figures), appropriately scaled down, were to be used in the calculator and HIC data and DUSC under co-payment prescription numbers used for script volumes for each strength and formulation when adjusting WAMTC estimates to reflect observed relativities.

The working group also determined that a responsible person-initiated price reduction would trigger a re-calculation and ad hoc review, if not all WAMTCs were statistically equal, on each occasion.

See ***Attachment B*** for details on how the process has changed from the January 2004 reviews going forward.

* Bootstrapping is a nonparametric technique of estimating the sample distribution for a statistic of interest. It is a re-sampling procedure, whereby samples of the same size as the original data are repeatedly drawn with replacement from the original data set and used to calculate the statistic of interest. Repeated a large number of times, the replication of the statistic of interest provides the empirical estimate of that statistic's sampling distribution. (Ref: O'Brien B and Briggs A, 2002, "Analysis of uncertainty in health care cost-effectiveness studies: an introduction to statistical issues and methods", *Statistical Methods in Medical Research*, 11, 455-468).

APPENDIX 1

THERAPEUTIC GROUP PREMIUM (TGP) POLICY

The policy outlined below appeared in the May 1998 PBS Schedule.

THERAPEUTIC GROUPING POLICY

The Therapeutic Grouping policy was announced as part of the 1997-98 Budget and took effect on 1 February 1998. The Therapeutic Grouping policy is an extension of the Minimum Pricing Policy and will encourage greater price competition between suppliers of drugs and make prescribers and patients more aware of the costs of medicines.

The Therapeutic Grouping policy applies within narrowly defined therapeutic sub-groups where the drugs concerned are of similar safety, efficacy and health outcomes.

Basically the policy operates by:

- the Commonwealth Government subsidising drugs within a defined therapeutic sub-group to the level of the lowest priced drug in the sub-group;

- suppliers of other drugs within the sub-group being able to set prices above the price charged by the supplier(s) of the lowest priced drug; and

- the patient paying the therapeutic group premium which is the price difference between the lowest price drug and the drug prescribed.

The policy applies to the following four therapeutic sub-groups:

- **H_2-receptor antagonists** (cimetidine, famotidine, nizatidine, ranitidine hydrochloride)

- **Dihydropyridine-derivative calcium channel blockers** (amlodipine besylate, felodipine, nifedipine) *(Note that the other calcium channel blockers, mibefradil dihydrochloride, verapamil hydrochloride and diltiazem hydrochloride, are not included in this sub-group)*

- **ACE inhibitors** (captopril, cilazapril monohydrate, enalapril maleate, fosinopril sodium, lisinopril, perindopril erbumine, quinapril hydrochloride, ramipril, trandolapril)

- **HMG CoA reductase inhibitors** (atorvastatin calcium, pravastatin sodium, simvastatin) *(Note that fluvastatin sodium is excluded from this sub-group and that no drugs in this sub-group have therapeutic group premiums)*

In some instances, a therapeutic group premium may apply for a particular form or strength of a drug for which other forms or strengths are the lowest priced the therapeutic sub-group.

'T' located immediately before an amount in the premium column indicates a therapeutic group premium which applies to that particular drug. 'B' located immediately before an amount in the premium column indicates a brand price premium which applies to that particular brand of the drug. If a brand of a drug which is subject to a therapeutic group premium also has a brand price premium, there will be two amounts shown on separate lines in the premium column, prefixed by 'T' and 'B' respectively. Both these premiums are payable by the patient.

Exemptions from therapeutic group premiums

Therapeutic group premiums will not apply to prescriptions written before 1 December 1997 and supplied up to 30 June 1998.

For all other prescriptions for benefit supplied from 1 February 1998 which involve a therapeutic group premium, the therapeutic group premium will apply unless the patient has been issued with an authority prescription for the drug.

For supplies made from 1 February 1998 to 30 June 1998 the authority prescription may be approved by telephone or in writing. For supplies made after 30 June 1998, the authority prescription must be approved in writing.

The circumstances in which an authority prescription may be obtained are:

- adverse effects and / or drug interactions occurring, or expected to occur, with all of the base-priced drugs; or

- transfer to a base-priced drug would cause patient confusion resulting in problems with compliance.

Where relevant, this wording has been incorporated without existing restrictions.

Separate codes have been established for these benefits when supplied on an authority prescription granting exemption from payment of the premium.

ATTACHMENT B
CHANGES TO WAMTC REVIEWS

Significant changes arising from analysis of the initial reviews by the PBPA in January 2004

Following the January 2004 WAMTC reviews, several changes to the process of a WAMTC review were made by the PBPA in December 2004 at the instigation of a joint Pharmaceutical Benefits Branch (PBB), Medicines Australia (MA) and Generic Medicines Industry Association (GMiA) WAMTC working group.

- A template making it clear what is involved in the making of price proposals was designed and is included at ***Attachment H***. Responsible persons applying for a price increase or exemption or making some other submission requiring PBPA consideration have the option of nominating a single alternative set of prices (contingent on their submission being rejected by the PBPA) rather than having current prices as the automatic fallback.

- Unsuccessful price proposals from responsible persons that do not cover the full range of a drug's formulations and/or strengths will be set aside if a point-to-point reduction in the WAMTC is required following the review. By setting aside such unsuccessful proposals, across-the-board reductions occur from the current prices and a responsible person that does not cover the full range of a drug's formulations and/or strengths is not disadvantaged for having proposed price reductions.

- The default when no price proposal is received was altered.

  In the January 2004 reviews, the default price, in the case of a nil response to the request for pricing proposals, was a DPMQ based on an unchanged price to pharmacist (which may have included a component for any previously applicable patient-paid premium).

  Following representations from industry and examination of the effects that a default price based on an unchanged price to pharmacist and an alternative may have in different circumstances, a new default provision when no price proposal is received involves subtracting previous BPs or TGPs from the current DPMQ to establish the entries that go into the WAMTC calculator.

  While this reduces the risk of a responsible person inadvertently finding that a drug's WAMTC is statistically greater than that of the benchmark drug, it increases the risk that a drug may unexpectedly become the benchmark drug (and is therefore not eligible for TGPs). Responsible persons with drugs in therapeutic groups are advised to analyse different scenarios that may occur and to take an active role in formulating pricing proposals.

- For the round of WAMTC reviews commencing with the ATRAs and PPIs in

December 2010, responsible persons will have the opportunity to submit sample dosage data from any approved source (see *Section 3 Data*). The sample data source selected for each of those reviews will then remain in force for that group for three years including three consecutive annual WAMTC reviews unless a responsible person succeeds in demonstrating its deficiencies and submits a better alternative.

Continuity of dosage data source should lessen avoidable variability and enable responsible persons to plan strategies in a more stable environment. Responsible persons seeking to challenge the use of a dosage data source within the three-year cycle must establish its deficiencies and submit a better alternative no later than 14 weeks before an annual WAMTC review of the group concerned. The PBPA Secretariat will then make the assessment of the different dosage data sources submitted, taking into account comments made by responsible persons and possibly other affected parties. See ***Attachment F*** for selection criteria for dosage data and the sub section of that attachment *Three-year cycle* for further details.

- A single cut-off for triggering ad hoc reviews applies 10 weeks before any PBPA meeting, and the data source used at the previous annual review continue to apply. Where no updated data are submitted, the PBPA Secretariat will obtain BEACH data or, dosage data from another provider if required.

- If an offer of a price reduction is received after the 10 week cut off, the brands of the same molecule will be subject to a price reduction or a Brand Premium can apply, while an ad hoc review for the WAMTC group will take place in time for the next available PBPA meeting, if the global test shows this is necessary.

- In discussions with industry around the introduction of the new WAMTC methodology, the most recent available complete four consecutive quarters of sample prescribing data are obtained along with combined Medicare Australia script information and DUSC estimates of under-co-payment script numbers. In this revision of the manual, it is further emphasised in some places that, even for consecutive annual reviews, sometimes there may be overlapping periods under consideration. This is generally inevitable for ad hoc reviews.

Other significant precedents or changes arising from WAMTC reviews

WAMTC reviews are conducted as much as possible according to the procedures and principles set out in this manual, and taking into consideration empirical evidence either submitted by responsible persons and any other interested parties, such as data providers, or otherwise available for consideration by the PBPA. As it is not possible to document everything that may happen in the course of a review, at times the PBPA will indicate a preferred way of dealing with a particular matter as a point of principle and this will result in future procedures following that precedent. Other procedures may arise from the application of an approach that follows similar principles which will go to the PBPA for endorsement. This section outlines some of these precedents and changes in procedures.

Notification of participating responsible persons and changes in listing arrangements

In a letter to responsible persons at the commencement of each review, the PBPA Secretariat provides a list of all the drugs and responsible persons participating in the review, i.e. all responsible persons with a known listing for at least one brand of a drug in the group on the date when the review will be undertaken by PBPA. This includes known responsible persons of new brands yet to be PBS listed, if they will be affected by the outcomes of the WAMTC review after listing. These responsible persons will be able to take full participation in the review, including the submission of price proposals.

As the PBS Schedule is now produced monthly, information about most new entrants would normally be revealed through the Schedule before price proposals became due. When revised Schedules came out every four months (up until December 2006), it was possible for new entrants to obtain a future listing for their brand and have offered a lower price without other responsible persons in the group becoming aware of their involvement in the review. It was felt that other responsible persons would need to know who was involved in the review in order to submit their price proposals as they may be able to anticipate there would be a lower price offer made by the new entrant, and possibly the establishment of a new benchmark WAMTC.

In the case of a new drug, participation begins only once four consecutive quarters of prescribing data are available.

While listings change each month, price changes can still occur only on 1 April, 1 August and 1 December in accordance with a provision in the Fourth Community Pharmacy Agreement.

Phasing-in of price reductions and other price changes around the time of a review

The PBPA has at times allowed price reductions arising from WAMTC reviews to be phased in, particularly when the 12.5% price reduction policy applied from August 2005 when the first new brand of any already PBS-listed drug was listed. When both types of reductions had to apply from a given day, the 12.5% adjustment was applied to the final prices arising from the WAMTC review. Consequently all drugs have been treated in the same fashion and their prices at the end of the phase-in period have been derived in a consistent manner.

The PBPA has recommended specifically in these cases that at least the dollar amount of the full 12.5% reduction must be taken straight away (this was subsequently set out in legislation in 2007), and that the phasing-in cannot occur over any longer than three consecutive price change days within a year of the review in question i.e. it must be phased in before the results of the next annual WAMTC review of the group is completed. Each request for phasing-in is examined by the PBPA on its merits to see whether extenuating circumstances do exist or whether the entire reduction should occur on the next price change day.

If in the course of a WAMTC review there is a change in dispensing fees or other adjustments related to drug price, the prices current at the start of the review are maintained as a starting point throughout the review. The relevant adjustments to incorporate such administrative price changes are made to the prices recommended at or immediately following the review.

Situations in which contingent price proposals may be submitted

In cases where a responsible person makes a submission to change the standard WAMTC calculations (see ***Attachment G*)**, the PBPA determines whether there are material effects beyond those automatically captured and whether a compelling case has been made for the specific proposal that a change occur. Usually the responsible person's submission, modified if needed to exclude commercial-in-confidence material, is circulated to other responsible persons and possibly other affected parties such as data providers for comment, and the PBPA Secretariat undertakes any further enquiries or investigations that are necessary.

A responsible person submitting a case to vary standard WAMTC calculations includes a price proposal in the event of success. Should the current prices not be appropriate in the event that the submission is rejected and standard calculations adopted, the responsible person may also submit a contingent price proposal for this circumstance.

The remaining responsible persons make their price proposal on the basis of the standard calculations applying, and may submit a contingent price proposal in case the PBPA accepts the argument for the proposed adjustment and current prices are not appropriate in that case.

Under this approach, apart from matters of brand or therapeutic group premiums and other areas where sole responsible persons of drugs have flexibility, reviews are finalised once a single submission to vary the standard calculations is either rejected or accepted in full.

However, if the PBPA determines that an adjustment to the standard calculation is warranted, but that it should be different from what a responsible person suggested, all responsible persons will be advised of that outcome and given an opportunity to submit another price proposal in those circumstances as they could not be anticipated in advance. The review is then finalised through an out-of-session decision by the PBPA.

If several competing proposals about how the standard calculations should be amended are submitted, because no more than one contingent price proposal is allowed, all responsible persons respond on the basis that the standard WAMTC calculations will apply. If the PBPA determines otherwise, all responsible persons are notified of the outcome and given an opportunity to make a price proposal suitable to their interests in those defined circumstances. The review is then finalised through an out-of-session decision by the PBPA.

In a similar manner, if a responsible person disputes the treatment of raw dosage data by

the PBPA Secretariat when it circulates a pre-calculation file and a request for price responses, a submission indicating the need to rectify material consequences may be made to the PBPA. Unusual dosages are examined for plausibility and not necessarily rejected just because they lie outside the recommended range. A contingent price response may also be forwarded in case the PBPA rejects the submission and accepts the assessment made by the PBPA Secretariat.

For the remaining responsible persons when a submission seeks to amend particulars of the raw dosage data, the price proposal relates to the pre-calculation file circulated by the PBPA Secretariat, and any contingent price proposal to the amended version proposed by a responsible person and circulated for comment.

Changes to the WAMTC calculator

A coding oversight meant that the original WAMTC calculator did not produce correct adjusted WAMTC variance estimates for any drugs after the tenth in a group. While this did not affect the accuracy of previous calculations and fairness of associated outcomes, appropriate changes were made at the start of 2006 and advised to industry for use from the April 2006 WAMTC reviews onwards. At the same time, the opportunity was taken to make a number of other amendments, such as ensuring that unadjusted WAMTCs are always sorted by upper 95% confidence bound and that the correct labels are attached to adjusted and unadjusted calculations on the *Summary* worksheet.

Making the most of the available data

Since the inception in January 2004 of WAMTC reviews under the revised methodology and purpose-built calculator, the same principles have been applied to the sample prescribing data and the possibility of adjustments to calculations. Some of these matters have been formalised through agreement with industry and ratification by the PBPA:

- as much as possible of the sample prescribing data is used without making inferences about incomplete, inconsistent or incorrect data;
- the WAMTC estimates are accepted as simplifying approximations valid in particular circumstances and are applied in the absence of convincing reasons why a proposed adjustment would be practicable and constitute a material improvement – for instance, if adjustments are to be made for the impact of authority scripts, it is essential to have reliable prescribing data relating just to them; and
- on clinical matters, the PBPA accepts the advice of the PBAC whenever it is required, and on matters to do with the registration of drugs, it accepts decisions of the TGA.

Sections 3.3 to 3.5, in the Data section, set out procedures that apply when:

- items have been deleted in the course of the four quarters over which prescribing data have been obtained – prescribing information is attached to the closest related item if possible, or otherwise on the basis of other strong empirical evidence; or
- questions arise about the extent to which data for various items should be pooled – the

amount of lost information is minimised where this is possible, and there is also pooling of prescribing information for drugs marked as bioequivalent or therapeutically equivalent in the *PBS Schedule*.

Impact of the PBS Reform package announced November 2006

A package of PBS Reforms came into effect from 1 August 2007 designed to obtain the best price for PBS-listed drugs. The reforms are intended to achieve a number of efficiencies for drugs operating in a competitive market would be subject to price reductions, and eventually move to a system where the price they are actually being sold at in the market would reflect the price that the Australian Government pays. This would facilitate the continued listing of new world-class life-enhancing drugs while not leaving patients more out of pocket.

Legislation was amended so that from 1 August 2007 drugs on the PBS would be separated into two groups, the F1 and F2 formularies, each subject to different pricing arrangements.

The F1 formulary would consist of drugs where there is only a single brand listed for a pharmaceutical item (containing the drug regardless of patent status) where the brands are not substitutable with other brands. There would be no statutory price reductions for these drugs and existing price linkages would be retained within this group.

Drugs where there is more than one brand listed and groups of drugs with brands that are interchangeable between patients would comprise the F2 formulary. Brands containing F2 drugs would be subject to statutory price reductions in addition to the requirement from August 2005 for a 12.5 per cent price reduction when the first new brand of a medicine is listed on the PBS. From 1 August 2008, these drugs would have a price drop of 2 per cent a year for three years (unless a 12.5% applies in April or August of the same year) if price competition between brands is low (F2A drugs), or a one-off price drop of 25 per cent where price competition between brands is high (F2T drugs).

Subsequently, phasing-in of the 25% reduction was agreed for lercanidipine, esomeprazole, lansoprazole, pantoprazole and rabeprazole among the calcium channel blockers and proton pump inhibitors. The actual amounts to be subtracted from the price to pharmacist for these five drugs on specific days were specified through the combined effect of Section 99ACK of the *National Health Act 1953* and the *National Health (Pharmaceutical Benefits) Regulations 1960.*

Drugs in the F2 formulary had already been separated according to the level of price competition between brands, on the basis of information supplied by those involved in the selling and purchasing of pharmaceuticals.

A more detailed Fact Sheet about the PBS Reform package prepared in February 2007 can be found at:
http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs_reform_02feb07.htm

The previous SSRIs plus group had a mixture of single-brand and multiple-brand drugs that were not all interchangeable at the patient level. Consequently the previous group was not subject to WAMTC review in August 2007 and is no longer operational following implementation of the PBS Reform package. It is nevertheless possible that smaller WAMTC groups each entirely within the same formulary will be formed from these drugs in future.

Similarly, diltiazem was delinked from the remaining calcium channel blockers (amlodipine, felodipine, lercanidipine and nifedipine) as it is not interchangeable at patient level with these other drugs. The four drugs in that former WAMTC group now form the calcium channel blockers therapeutic group and are still subject to annual WAMTC review.

WAMTC reviews for each of the six current groups (the ATRAs are all in the F1 formulary while each of the remaining groups lies within the F2 formulary) and any new ones that might subsequently be formed will continue as part of the PBPA's annual cycle of price reviews. Modifications will be made to the standard WAMTC calculations for the proton pump inhibitors and calcium channel blockers to take full account of the way in which certain statutory price reductions are being phased in.

ATTACHMENT C
ADJUSTMENTS, EXEMPTIONS, EXCLUSIONS

Overview

The WAMTC methodology is intended to be applied to a group of drugs that have been accepted by the PBAC on the basis that they provide the same or similar health benefits on a population basis. The methodology is intended to account for different usage practices in the market place compared with the formal clinical trial situation.

These differences could be due to one or more reasons after a subsidised listing has occurred. For example:

- one drug might be perceived by prescribers as often needing a higher/lower dose;
- the way the drug is prescribed, for example, mainly by specialists;
- a drug might be used at a higher dose as it is mainly reserved for resistant patients;
- recent clinical trial evidence may suggest new uses and/or different dosage regimes.

The inclusion of new drugs or removal of drugs from a WAMTC group will be made by the PBPA and be based on recommendations from the PBAC regarding listing on a cost minimisation basis with one or more drugs in the WAMTC group.

Where the PBPA proposes the formation of a new WAMTC group that has not previously been subject to this pricing methodology or the addition of a new molecule to an existing WAMTC group, the affected responsible persons will be given sufficient notice and a formal opportunity to provide comment on the proposal. Drugs in the F2 formulary can only be subject to WAMTC review if they are a part of a therapeutic group that the Minister has designated.

It is important for responsible persons to be aware that the PBPA and PBAC have different roles in the assessment of pharmaceuticals. To make submissions seeking a departure from the standard WAMTC calculations, responsible persons must consider whether the PBAC or PBPA is most appropriate to make the decision:

- on matters of a clinical nature including the relative performance of drugs, decisions are made by the PBAC;
- for non-clinical evidence, the PBPA determines whether a drug should be fully exempt, partially, or have its WAMTC adjusted in a particular manner.

Where it is believed that real differences in health outcomes have become evident over time, then the onus is on the responsible person of the drug to provide the appropriate evidence to the PBAC demonstrating superiority and acceptable cost-effectiveness. Until the PBAC makes a positive finding in this regard and conveys this to the PBPA, the

previous decision(s) of the PBAC on clinical matters will stand and continue to be acted upon. Therefore, pricing reviews by the PBPA will not be put on hold while an exemption request is under consideration by the PBAC.

The PBPA will examine requests for exempting drugs from the standard WAMTC calculations or adjusting those calculations where it is claimed that the available dosage data do not adequately reflect the true marketplace experience:

- as prescribing data from commercial sources cover only GP activity, if specialists undertake substantial levels of prescribing for some drugs that may lead to a change in overall WAMTC relativities, empirical evidence will be closely considered;
- similarly if authority scripts are significant in number and their incidence varies across different drugs, it may be possible to make out a case for adjusting the basic WAMTC calculation.

These examples are not exhaustive. There may be other circumstances for responsible persons to consider when seeking an adjustment. The onus is on the responsible person to submit its case to the PBPA.

In these situations the responsible person may seek an adjustment by the PBPA rather than an exclusion of the drug(s) from the WAMTC group. An adjustment to the standard WAMTC calculation will be suggested to the PBPA by a responsible person on the basis of additional available empirical evidence, and may be accepted in full or modified to a degree.

One of the reasons for an exemption of a drug from WAMTC calculations due to data source issues is when it has a low WAMTC consistently, but the sample dosage data have insufficient observations for it to become the benchmark drug. To apply for an exemption on such grounds, a responsible person would need to demonstrate that all data sources are problematic, otherwise the data source could be changed.

Other responsible persons will normally have an opportunity to comment on the aspects of submissions potentially affecting their interests that are not commercial-in-confidence.

Adjustments

Where a responsible person can show evidence that available dosage data do not reflect prescribing habits over the specified period for one or more strengths of their drug, an adjustment to the WAMTC calculation can be made to that proportion of usage that is not represented by the available dosage data.

For instance, as commercially available dosage data sources provide information only on the prescribing behaviour of GPs, if specialists play a significant role for some drugs and the addition of information about their prescribing may alter relativities between estimated monthly average treatment costs for some drugs, responsible persons may choose to make a submission to the PBPA that supplies evidence of the differences and suggests what

conclusions should be drawn from that material.

Prima facie, where the potential material impact of authority scripts has been established it is possible to consider treating different authority prescriptions as representing a different product. Establishing a true effect involves not only that authority scripts occur in sufficiently large number to warrant further attention, but also some evidence of the possibility that they affect the benchmark drug more than the other drugs in the group and thereby may be resulting in differences between WAMTCs for each drug being exaggerated in the simple calculation made by the software because that of the benchmark drug is depressed to a greater extent than the others. Provided that separate dosage data are available for authority scripts, it would be possible to add just a few major additional groupings of pack numbers and the relevant costs when dispensed simultaneously (authority prescriptions are typically concentrated on a small number of quantities) and continue to apply the current calculator.

Exemptions

Where a particular strength of a drug has been listed on a cost-effectiveness basis for a unique indication, this strength will usually not be included in the WAMTC calculations and the sample dosage data entered into the WAMTC calculator will be adjusted to reflect that. For instance, the 40 mg strength of esomeprazole was listed on this basis and therefore following an application by the responsible person that sets out detailed usage information, only usage of its 20 mg strength is considered in WAMTC calculations. In some cases, it may be possible to get a reasonable or very good estimate of the extent of usage of these strengths that is not cost-effective and include this proportion in WAMTC calculations.

Where a particular drug has approval for use in relation to a unique indication and it is possible to identify incremental usage patterns on that account, it may be possible to make a case for excluding this incremental usage from the WAMTC calculations. As some drugs will have multiple indications, in these circumstances it is important to establish average (inappropriate) usage levels for that indication of the other drugs and subtract these from the incidence of prescribing for the drug with the unique indication.

If an adjustment cannot adequately be made to the calculation to reflect the true usage patterns for a particular formulation and/or strength of a drug, a responsible person may present a case to the PBPA for exemption for that particular strength, or for a particular segment of dosage data. This does not exclude the entire drug from the WAMTC review.

For exemption of part of the usage for a drug, it needs to be demonstrated that the other drugs in the class would not be similarly as safe and as effective when used in that way. If just one drug in a group were approved for use to treat a particular indication, its responsible person would need to provide evidence to support making the specific adjustment being proposed.

Exclusions

The WAMTC methodology applies to drugs that have been accepted by the PBAC as providing the same or similar health outcomes.

When a responsible person has evidence that a drug may no longer be comparable in terms of efficacy and safety with the drugs in the WAMTC group, a formal submission to the PBAC, and a subsequent positive recommendation of acceptable cost effectiveness, is the avenue for excluding the drug from the WAMTC group.

It is the responsible person's responsibility to make such a submission to the PBAC. The PBPA will not assess the clinical evidence. The current advice from the PBAC will stand and a drug's current WAMTC situation will persist until such time as a positive recommendation from PBAC has been made.

The PBAC has accepted that a difference of 15% between the market relativity and the clinical trial relativity would be an indication of a reason for clinical review.

Timing of submissions

Responsible persons may make submissions relating to exemption or adjustment methodologies in relation to their drugs to any meeting of the PBPA. They need not wait for a WAMTC review to place such evidence before the PBPA.

In the course of a WAMTC review, such submissions are due at or before the time when responsible persons provide their pricing proposals in response to the initial WAMTC calculator results. Where the interests of other responsible persons may be affected, a copy of the submission, amended as required by the responsible person to exclude matters that are commercial-in-confidence, is circulated to the other responsible persons in the WAMTC group for comment during the period when WAMTC calculations are being re-run on the basis of price responses and/or PBPA papers are being finalised.

Examples of previous submissions to the PBPA and the PBPA decisions

Both the WAMTC manual and the therapeutic relativity sheets will be updated when there are successful applications for exemptions, exclusions and adjustments.

Responsible persons seeking exemptions, partial exemptions or adjustments to the WAMTC calculation need to consider the basis for the claim and which body would be more relevant to consider the claim. In addition to the advice in this manual, responsible persons can seek the advice of the PBPA or PBAC Secretariat. Some examples of past claims to the PBPA are discussed below.

Complete exemption (exclusion)

- Request to exclude a drug from the group because it has a higher use by specialists, it is used by a higher proportion of males, it has a different age distribution and it has a higher proportion of original prescriptions. This was rejected by PBPA on the basis that evidence of use by different groups of patients in the market place on its own is not sufficient to claim a full exemption. For exclusion from the group, it is more suitable to provide new clinical evidence of superiority to the PBAC.
- Request to exclude the drug from the group on the basis that it was not interchangeable with other drugs in the group. This was rejected by the PBPA on the basis that WAMTC drugs are not necessarily 'interchangeable' (whereas this is a requirement for therapeutic group drugs).
- Request to exclude the drug from the group because it was intended to present a submission to the PBAC. This was rejected by the PBPA on the basis that the current advised situation applies until further advice is received from the PBAC to change this.

Partial exemption

- Request to exclude the volume of prescriptions approved under the authority provisions because this indicated that the drug was unique. This was rejected by the PBPA on the basis that the request was not supported by evidence.
- Request to exclude all of the patients in a certain category because the percentage of use in that category was higher than for a competitor drug. This was rejected by the PBPA on the basis that the request for a particular adjustment was not reasonable in the light of the evidence provided and that the other drugs could be used in the same setting.
- Request to exempt a higher strength of a drug on the basis that this was used in a unique setting and that it had been recommended on a cost effectiveness basis compared with the lower strength. This was accepted by the PBPA.
- Request to exclude two thirds of use of a particular strength because the drug is used differently and uniquely. This was rejected by the PBPA on the basis the request had not been supported by evidence.

ATTACHMENT D
FREQUENTLY ASKED QUESTIONS

Q. How are sample prescribing data cleaned?

A. Incomplete or incorrect entries from the sample prescribing data (for instance, where a strength and formulation is given but not the daily frequency or where a strength that is not listed on the PBS appears) are set aside as invalid and the plausibility of unusual dosages is checked by a medical or pharmaceutical advisor to the PBPA Secretariat.

Responsible persons may have raised matters about individual entries in the raw sample data when submitting their grouping of that information, or may do so during the period before the despatch of requests for price responses.

In general, there is a presumption that the recorded sample data are accurate unless there is strong evidence that they cannot be. For instance, a dosage that would most likely harm a patient would be rejected, but not necessarily one that is higher or lower than what is recommended or appears in the approved product information.

In relation to fractional dosages, practicality is the major factor. Where tablets can be scored and divided, plausible dosages, particularly one-half and other easily-achieved divisions, will be accepted. In addition, dosages such as “1 tablet three times a week” will be converted to a daily dosage of a decimal fraction (closely approximating three-sevenths in the example just mentioned).

Q. What price is used when the WAMTC calculator is run initially, and pricing proposals are requested?

A. The current cost to the Australian Government, taken from the latest PBS Schedule, or as a result of a reduction that triggers an ad-hoc review. This is the dispensed price (DPMQ) minus any TGPs or BPs or SPCs. Note that patient co-payments are not subtracted.

Q. If I do not submit a price proposal after the initial WAMTC calculation, what happens?

A. As in the first run of the calculator, the previous brand premium or TGP or SPC will be subtracted from the dispensed price for maximum quantity and will be used as the basis for the calculation. Note: depending on other price proposals received, it is possible that this may result in a drug with a previous TGP becoming the benchmark drug and no longer being eligible for a TGP. Responsible persons who currently have a TGP are therefore advised to closely examine the situation in their group.

This default was agreed after strong representations in its favour from industry, and the circulation of material highlighting the effects it and an alternative can have in particular

circumstances.

Q. Where a drug's WAMTC is different from that of the benchmark drug after price proposals have been received, what degree of price reduction is required?

A. In this context, 'different' means that the global chi-square test for equality of all WAMTCs has proved negative and the pairwise z-test has indicated that the drug's WAMTC is significantly greater than that of the benchmark drug.

As a consequence, a point-to-point reduction is required to bring the drug's WAMTC down to the level of the benchmark drug's WAMTC. The level of across-the-board price reduction required to achieve the same WAMTC as the benchmark drug can be found among the entries from C5 and immediately below on the WAMTC calculator's *Summary Sheet* worksheet. The degree of price reduction needed for the WAMTC to become statistically no different from that of the benchmark will be somewhat less but of no relevance once price proposals have been received and entered in the calculator.

Unsuccessful proposals of reductions by responsible persons not supplying the full range of strengths and/or formulations will be set aside in assessing what reductions are required to achieve the benchmark WAMTC.

Sole suppliers of a drug have the flexibility to achieve the required WAMTC by applying greater levels of reduction at some formulations and/or strengths and lesser ones or maintaining current prices at others, provided that the overall pricing scheme remains within the normal guidelines for pricing at different strengths.

Multiple suppliers face the same across-the-board level of reduction at each formulation and/or strength.

Q. How is the benchmark drug determined?

A. The benchmark drug will be the one with the lowest 95% upper confidence bound, provided that there are at least 65 scripts in the sample dosage data.

In these circumstances, for the final calculation which determines the lowest cost to the PBS after price proposals are received, as TGPs no longer apply, all drugs are eligible to be the benchmark, and at least one drug in the group must be supplied at that price without a TGP.

Q. Is a drug with fewer than 65 scripts in sample dosage data excluded from the WAMTC review?

A. No. A drug with fewer than 65 scripts in the sample dosage data will not become the benchmark drug. However, the WAMTC of that drug is still calculated and assessed

against the WAMTCs of the other drugs. If its WAMTC has the lowest 95% upper confidence bound of the group, a new calculation will be run, without that drug, to determine the benchmark drug. If, on the other hand, that drug has a WAMTC statistically significantly higher than that of the benchmark drug, it will be required to take a price reduction, in accordance with the process for all other drugs in the group.

Q. In what ways can the standard WAMTC calculation be amended to reflect the dispensing of large amounts of authority scripts?

A. Medicare Australia data that are used for realignment among the various strengths of a drug through adjusted WAMTC calculations records a single script each time a pharmacist dispenses several times the maximum quantity to a patient on a fairly high dosage. Typically, such occasions are heavily concentrated on two or three packs being dispensed simultaneously.

If such authority scripts occur frequently, the accuracy of WAMTC estimates will suffer as the higher cost to the Australian Government in these instances isn't reflected in the standard calculations. Some responsible persons may expect that there will be a material effect on WAMTC relativities and the circumstances in which price adjustments for individual drugs including theirs are necessary.

Should there be satisfactory dosage data available separately for authority scripts (both in relation to plausibility for individual patients and relative overall incidence), an affected responsible person could attempt to make a case for amending the standard WAMTC calculation. For instance, it might be argued that materially better WAMTC estimates would be obtained by adding the dosage data and associated pricing information for the most common authority scripts as new entries on the worksheet for each drug.

Based on the supporting evidence provided and comments provided by other responsible persons as well as any further investigations by the PBPA Secretariat, the PBPA determines whether there appear to be material effects affecting WAMTC relativities, and if so, how the standard WAMTC calculations should be modified. In these cases, in addition to making a price response based on the standard calculations, the remaining responsible persons may also submit a contingent price response in the event that the PBPA accepts the argument for a specific adjustment one of them has suggested.

Q. Are responsible persons required to offer the same level of price reduction for each formulation and strength of their drug?

A. In putting together price proposals, responsible persons have quite a deal of flexibility provided that they remain within the normal PBPA guidelines for pricing at different strengths.

If after price proposals are received, the global test indicates some differences among

estimated WAMTCs of drugs and a drug that has multiple responsible persons has an estimated WAMTC significantly higher than that of the benchmark drug, the same percentage level of reduction at DPMQ is applied across all strengths and formulations in order to match the WAMTC of the benchmark drug. This prevents any ratcheting downwards because the strategic interests of different responsible persons of a drug happen to vary.

Sole suppliers required to undertake a point-to-point reduction to match the WAMTC of the benchmark drug following a review, are allowed to vary reduction levels at different strengths and formulations provided that their final suite of prices remains within acceptable norms and results in a reduced estimated WAMTC as required.

Q. When can one or more strengths be excluded from any price reductions that are offered by a responsible person?

A. In determining price responses, responsible persons may concentrate any reductions offered on one or more strengths/formulations provided that their proposals remain within the normal guidelines for pricing at different strengths.

Sole responsible persons of drugs required to achieve a point-to-point WAMTC adjustment following a review may leave prices at one or more strengths/formulations unaltered as long as their suite of prices produces the estimated WAMTC sought and conforms with the PBPA's pricing guidelines.

Q. When the WAMTC calculator is run the second time, after price proposals are received, what prices are used?

A. This calculation compares the proposed costs to the Australian Government using the latest available sample dosage data and overall aggregate Medicare Australia and DUSC script numbers as the reference points. The lowest proposed price for each drug and strength entered on the price response template is used (see ***Attachment H***).

Where no price proposal is received, any previous brand premium or TGP or SPC will be subtracted from the previous dispensed price for maximum quantity and then used as the basis for the calculation.

Price proposals cannot involve premiums of any kind as the benchmark price is not yet established, nor the lowest price at which each formulation and/or strength of every drug is to be offered.

Q. What happens if my lower price proposal does not result in the WAMTC being statistically equal to that of the benchmark drug? Can I propose another price?

A. No. Where the drug sits in relation to the benchmark at the end of the calculations will be determined by the price proposals received.

If a responsible person proposes a reduction leaving a WAMTC that is still significantly higher than the benchmark drug's (which may have moved up or down), then it is required to reduce further to the WAMTC point estimate of the benchmark drug. There is no second opportunity to reduce to a lesser level that leaves the drug's WAMTC above that of the benchmark drug.

Unsuccessful proposals of reductions by responsible persons not supplying the full range of strengths and/or formulations will be set aside in assessing what reductions are required to achieve the benchmark WAMTC.

Q. When can we add Brand Premiums (BPs)?

A. After the PBPA meets to determine the lowest price offers and the benchmark drug, responsible persons are asked to either meet the lowest price at each formulation and/or strength for their drug, or establish a BP of whatever magnitude they wish.

At each formulation and/or strength, the drug must be available at the lowest proposed price and hence there must be at least one brand without any BP. By definition, these premiums cannot be established until after the lowest proposed prices for that drug have been determined.

Q. When can we add Therapeutic Group Premiums (TGPs)?

A. A TGP may only be added to a drug that is not the benchmark drug in a specified therapeutic group of drugs (see ***Section 1.2*** for detail on therapeutic groups).

The TGP policy enables sole responsible persons of a particular formulation and/or strength of a drug that is not the benchmark drug to require an additional payment by patients. They are notified of their options after the PBPA has determined the benchmark drug and the lowest prices at each strength and/or formulation for every drug.

Where the drug's WAMTC is statistically equal to that of the benchmark drug, there is no limitation on the level of the TGP. However, where the drug's WAMTC is statistically greater and the responsible person does not wish to reduce the cost to the Australian Government, at least a floor TGP level will be necessary to achieve the required reduction in the drug's WAMTC.

Q. In what circumstances can a responsible person impose a special patient contribution?

A. Special patient contributions may only arise if there is a disagreement between the

responsible person and the Australian Government about the price to be paid for a brand of a pharmaceutical item that cannot be resolved by the responsible person imposing upon patients a brand premium or therapeutic brand premium that makes up the difference.

In such cases, the Minister decides whether a condition of continued listing of the drug on the PBS is acceptance of the price the Australian Government will agree to. Alternatively, the Minister may determine that additional circumstances apply, such as the desire not to disadvantage a group of patients for whom the drug brings particular benefits, and point to continued listing arrangements involving a special patient contribution under which patients will only have access to the drug if, in addition to the usual co-payment, they pay a further amount equal to the difference between the price sought by the responsible person and the amount the Australian Government is willing to pay.

Q. If an initial WAMTC calculation is run, and no price reductions are required and no price reductions are proposed, how is that in the second run of the calculator some price reductions may be required? What has changed?

A. At the initial WAMTC reviews under the new methodology, this result was possible for TGP group in certain circumstances involving changing prescribing patterns where there were previously TGPs and responsible persons required a minimum price level, whether from the Australian Government alone or with a patient contribution.

Following the change in the default provision for a nil response, such an outcome will not be possible if no responsible person advises a price proposal. However, responsible persons should be aware that a successful application for a price increase may sometimes result in a previously negative global test outcome turning to positive and leading to one or more pair-wise comparisons with the WAMTC of the benchmark drug indicating that point-to-point reductions are now necessary.

Q. What happens if a responsible person wants to list a new brand of a drug in a WAMTC group at the current list price?

A. The listing would be the same as any "new brand" situation, and could be subject to the minimum 12.5% price reductions applying for the first new brand of a listed brand of drug with the same manner of administration or in the same Therapeutic Group and have the same manner of administration. No ad hoc WAMTC review is triggered in either case.

Q. What happens if a company wants to list a new, or current, brand of a WAMTC drug at a price lower than the current list price?

A. Except where there is a compulsory minimum level of decrease required, and it is flowed on to all the other drugs in the reference group, the offer of a lower price for a WAMTC drug will potentially trigger a full ad hoc review.

Using the same dosage data source as at the previous annual review for that group (but over the most recent timeframe of four continuous quarters available), an initial WAMTC calculation is made to determine if there are any statistically significant differences between the drugs' WAMTCs. If no difference is detected in the global test, no further action is taken, other than to establish whether other responsible persons of the drug for which a lower price is offered will adopt the lower price or impose a brand premium. If a difference is detected, then a full ad hoc review proceeds and relevant responsible persons are asked for their price proposals.

Note that the drug which initiates the ad hoc review through a price reduction does not necessarily need to become the benchmark drug. It is sufficient that changes in prescribing patterns reveal that the cost to the Australian Government of treatment with each drug is no longer the same.

Q. What happens if a company lists a new brand of a drug before the current WAMTC review is finalised? How do these companies participate in the review?

A. From 1 December 2006, monthly PBS listings were introduced. This means that new brands of drugs may be more readily listed during a WAMTC review. Those responsible persons who apply to list brands before the commencement of a review will be included in the review, while responsible persons listing new brands after the commencement of the review will be advised of the review, but not asked to submit price proposals. Any price changes resulting from the review will flow on to all the newly-listed brands.

For reviews beginning in February for PBPA consideration in April, and price changes normally effective on 1 August, the continuing responsible persons listed on 1 February or that have already lodged a new listing to take effect before the review occurs will be included.

For reviews beginning in June for PBPA consideration in August, and price changes normally effective on 1 December, the continuing responsible persons listed on 1 June or that have already lodged a new listing to take effect before the review occurs will be included.

For reviews beginning in October for PBPA consideration in December, and price changes normally effective on 1 April, the continuing responsible persons listed on 1 October or that have already lodged a new listing to take effect before the review occurs will be included.

Q. If an ad hoc price reduction offered on a drug changes the benchmark WAMTC, is that price offer disclosed to the other responsible persons?

A. At a minimum, other responsible persons of the same drug would be notified and asked

if they want to drop to the new benchmark price at the formulations and/or strengths concerned, or have a brand premium.

If the WAMTCs of the other drugs in the group are found not to be different from the new benchmark's WAMTC, the responsible persons of those other drugs will not be notified of the price offer. If there are differences, an ad hoc review proceeds, in which case responsible persons will be able to infer the level of reductions offered for individual strengths from the entries in the WAMTC pre-calculation file that they receive when they are asked for their price proposals. It is assumed the responsible person offering the reduction is aware that this may happen as part of the WAMTC process.

Q. What happens when a new drug is launched, that would form part of an existing WAMTC group?

A. If a new drug is added to a WAMTC group, it will not be included in any WAMTC review until at least four continuous quarters' dosage data are available for that drug. The inclusion of a new drug in a WAMTC group is a decision made by the PBPA and is supported by PBAC findings or advice. Responsible persons are notified of the inclusion of the new drug at the start of the review.

Q. As the responsible person of a benchmark drug, I'm requesting a price increase. When I run the proposed price through the WAMTC calculator the global test indicates that the other drug's WAMTCs are no longer statistically different from that of our benchmark drug. Will they no longer have to take a price reduction?

A. If all other things remained equal, and the request for a price increase were granted, it is possible that the global chi-square test would now show no difference between the WAMTCs of the drugs in the group, and thus no further price reductions would be required.

However, it may not be worth the risk to another responsible person whose drug's WAMTC is initially statistically higher than that of the benchmark drug to hope that the benchmark price will increase to a particular point that negates the need to offer a lower price.

The PBPA considers requests for price increases according to its usual criteria. If the PBPA does not agree to a price increase or accepts one that is not large enough to alter a drug's WAMTC status compared with that of the benchmark drug, a reduction in the drug's WAMTC to the point estimate of the benchmark drug's WAMTC will be necessary. Each responsible person of other drugs would have to consider the risk and consequences of possibly having to lower its prices to match the point estimate of the benchmark drug when deciding what price proposal it should make.

A price proposal is a formal offer in the sense that should the proposed price be the lowest

at a particular formulation or strength, the drug will need to be available at that price for that PBS item. The price proposal will not be set aside because of a subsequent increase in the price of the benchmark drug.

Q. What is required to propose a price increase?

A. As for any request for a price increase, the proposal must be accompanied by a PB 11(b) form, which indicates current cost of goods and manufacture information. The PBPA will determine the extent of the increase granted, if any, based on that information if there are no lower prices available for that drug.

A PB 11(b) form is required when responsible persons are seeking an increase in the cost to the PBS. As a component of any TGP or BP or SPC amount is included in the current price to pharmacist, an increase in the cost to the PBS (i.e. the cost borne by the Australian Government) may not translate to an increase in price to pharmacist for those drugs. However, a PB11(b) form will still be required where, in the price proposal template (***Attachment H***), the price response in column 3 is greater than the price in column 4, 'Default entry where no response is received'. At this stage, responsible persons are proposing prices to be borne by the Australian Government, and so no TGPs or BPs can yet be included. Opportunities for adding premiums will be outlined to responsible persons after the PBPA meeting, where the benchmark WAMTC and benchmark prices for the drugs are determined.

Note: if other responsible persons of the same drug have proposed a lower price, this is the price the PBPA will accept, and the remaining responsible persons of that drug will instead have an opportunity to add BPs after the WAMTC review if desired.

Q. What kinds of costs may not be included in the cost of goods that is recorded on the PB11(b) form when a price increase is sought?

A. The cost of goods relates to manufacturing or sourcing costs such as landed cost, packaging, drug content, quality assurance, plant and equipment, manufacturing overheads and TGA fees.

They do not include corporate expenses such as the costs of litigation in relation to a drug or educational or promotional activity related to the drug.

Q. How is the dosage data source determined for a regular annual WAMTC review?

A. The most up-to-date twelve months of quarterly Medicare Australia and DUSC script volume data are obtained when a review begins and this determines the period over which the review will take place. From time to time overlapping data periods may need to be used for consecutive annual reviews if four fresh quarters' data are not available at the commencement of the review. Dosage data over this period are sought from responsible

persons by the PBPA Secretariat.

At the start of each three-yearly cycle, responsible persons may propose dosage data from any source from which WAMTC point and variance estimates can readily be calculated. If more than one data source is proposed, the PBPA Secretariat will determine the most appropriate source, through assessment in accordance with the criteria set out in ***Attachment F***, as well as consideration of comments supplied by responsible persons and possibly other interested parties. In the event that no updated dosage data are submitted from any responsible person for the period covered by the review, the PBPA Secretariat will have obtained relevant BEACH data or, dosage data from another provider if required.

The dosage data source that is used at a WAMTC review at which responsible persons have been free to propose any viable source will normally be maintained for three years. However during that period a responsible person can request that the PBPA consider a substitution by first demonstrating that adjusted and unadjusted WAMTCs for a majority of the drugs in the group with multiple strengths and/or formulations are more than two standard deviations apart (based on estimated adjusted WAMTC variance). In relation to the proposed replacement data source, the responsible person needs to show that for both a majority of these distant drugs in the group and a majority of drugs with multiple strengths and/or formulations, the adjusted and unadjusted WAMTCs are closer together in terms of the estimated standard deviation of the adjusted WAMTC.

Q. How is the dosage data source determined for an ad hoc WAMTC review?

A. The PBPA has determined that the dosage data source for an ad hoc WAMTC review will be the same as that for the preceding annual review. Where possible, the updated dosage data should be supplied by the responsible person triggering the review through its lower price offer. Alternatively, the PBPA Secretariat will approach the other responsible persons to supply the data. In the event that no updated data are obtained from responsible persons, BEACH data or, dosage data from another provider if required will be made available through the PBPA Secretariat.

As for an annual review, the most up-to-date Medicare Australia and DUSC script volume data are obtained when the review begins, and this determines the time period over which the review will take place. The PBPA Secretariat will use the latest available four quarters' continuous data. This means that from time to time overlapping data periods may need to be used.

Q. Can a responsible person still submit BEACH data, even though the PBPA Secretariat will already have it as a back-up?

A. Yes. BEACH data is commercially available, and is one of the sources approved for use in the WAMTC process. It may be in a responsible person's best interest to assess this data source against others to help decide which data source to submit.

Q. After receiving a positive recommendation from the PBAC to list my drug as cost effective (not cost minimised), the drug is no longer part of the WAMTC group. Do I have to wait until the next annual review of the WAMTC group to propose a change in price?

A. No. As with any positive recommendation from the PBAC, price negotiations are subsequently undertaken with the PBPA Secretariat, and presented to the PBPA at their ensuing meeting. A price change would then most likely take effect from whichever of 1 April, 1 August, or 1 December follows the PBPA meeting most closely, and still leaves time for price changes to be processed before the deadline that applies.

Q. How does the PBS Reform package affect WAMTC reviews?

A. The continuation of reference pricing for groups of drugs within the F1 and F2 formularies was made clear both in the public announcement of the reform package in November 2006 and in the subsequent release of additional information in February 2007 (http://www.health.gov.au/internet/main/publishing.nsf/Content/pbs_reform_02feb07.htm).

As such, WAMTC reviews will continue to be conducted in accordance with the PBPA's annual cycle of price reviews.

Adjustments will be made to the standard calculations involving the proton pump inhibitors and calcium channel blockers as some brands of pharmaceutical items in both groups are having the amount of the statutory price reduction required on 1 August 2008 phased in over a number of years.

Q. If a responsible person disagrees with the sample dosage information sent out when the PBPA Secretariat requests price responses, what action is still open to it?

A. In arriving at the cleaned sample dosage data in relation to which price proposals are sought, the PBPA Secretariat carefully considers responsible persons' views and obtains medical and pharmaceutical advice as necessary.

A responsible person that disagrees with a material matter in the cleaned dosage data may make a submission to the PBPA setting out what the sample dosage data should be and why, and indicate a contingent price proposal in case this submission is rejected and the current prices are not appropriate as a response by the responsible person under the standard WAMTC calculations. Other responsible persons will have an opportunity to comment on the submission and also submit contingent price proposals (in this case, if there has been an adjustment to the standard calculations) if they wish.

Q. How does a responsible person go about changing a prescribing data source that has just been adopted for three years?

A. First, a change can only be made if the data source determined by the PBPA through open competition is showing likely deficiencies. Using sample prescribing data from four consecutive quarters, a majority of the drugs with multiple strengths and/or formulations must have adjusted and unadjusted estimated WAMTCs distant by at least two estimated adjusted WAMTC standard deviations. Otherwise the possibility of replacement does not arise.

Second, the responsible person requesting a change must also propose an alternative data source that in the same twelve-month period has both:

- lower normalised distances between estimated adjusted and unadjusted WAMTCs for over half the drugs whose estimated adjusted and unadjusted WAMTCs are at least two standard adjusted WAMTC deviations apart using the default data source; and
- lower normalised distances between estimated adjusted and unadjusted WAMTCs for a majority of the drugs in the group with multiple strengths and/or formulations.

Data indicating defects of the current data source and superiority of the proposed replacement as set out above must be submitted to the PBPA Secretariat at least 14 weeks before the start of any WAMTC review. Such data may be presented at any time and if this occurs other than just before when a WAMTC review is about to begin, any resultant change of data source comes into effect following the PBPA's examination of the Secretariat's assessment of the claims made by the initiating responsible person and any comments made by others in relation to them.

Q. If a responsible person seeks an adjustment to the standard WAMTC calculation, what protection is there against excessive price reductions if its submission is rejected by the PBPA?

A. Decisions about adjustments to the standard calculations are made by the PBPA at the review after other responsible persons have had an opportunity to comment on the proposed changes and the PBPA Secretariat has investigated the proposal.

A responsible person proposing an adjustment submits price responses based on their proposed amendments to the standard calculations being adopted. If current prices would not be submitted in the event that the PBPA rejects the submission, those that would can be entered as a contingent response on the price response template.

This means that, apart from the flexibility allowed in relation to brand premiums and therapeutic group premiums, and to sole responsible persons of drugs where a point-to-point reduction to the WAMTC of the benchmark drug is necessary, future prices are determined at the review if either the standard WAMTC calculation or proposed adjustment is judged to be appropriate by the PBPA.

In the event that the PBPA decides that an adjustment should be made to the standard WAMTC calculations but ought to be different from what the responsible person has proposed, all responsible persons will have an opportunity to make a price response in the circumstances to apply. The PBPA will then finalise the review in an out-of-session decision.

Q. If a submission is made to the PBPA, will commercial-in-confidence material in it be circulated to other responsible persons?

A. Responsible persons are requested to indicate whether any material in their submissions should be treated as commercial-in-confidence, and in that case preferably make available an alternative version excluding such material for circulation to other responsible persons for comment.

As transparency is fundamental to the new WAMTC methodology, in the absence of any indication to the contrary from responsible persons making submissions, it is assumed that material in submissions is for circulation.

If a responsible person determines that all the material in a submission is too sensitive for circulation, other responsible persons will receive a précis of the proposal without any supporting evidence and be invited to comment. The PBPA Secretariat undertakes whatever inquiries or investigations are required in these circumstances and may present advice and options or recommendations to the PBPA.

Q. What scope is there to correct any past PBPA decisions on WAMTC matters found to be based on errors?

A. In the event that an error is not detected by any of the numerous parties involved until the period immediately following a WAMTC review, the PBPA may agree to reconsider decisions made and rectify matters out of session, or decide upon some other remedial course of action.

Once new prices have been agreed following a WAMTC review and implemented, they become the basis on which sample prescribing data for periods covered in future reviews are converted into estimated monthly treatment costs per patient and compared.

Q. In what circumstances can a WAMTC group be formed?

A. Following implementation of the PBS Reform package, all the drugs involved in any form of reference pricing within a group must either be in the F1 formulary, or be interchangeable at the level of the individual patient in the F2 formulary.

The initiative to suggest formation of a new group may be taken by individual responsible

persons who feel that the estimated average monthly treatment cost per patient will provide a fairer basis for pricing than fixed dosage relativities determined by the PBAC on the basis of clinical trial evidence.

As the PBAC routinely indicates when drugs may be suitable for WAMTC reference pricing, the PBPA may also give further consideration to the practicability of such pricing in specific groups bound together by listing on a cost-minimisation basis, or seek from the PBAC additional advice about interchangeability at the level of the individual patient.

Affected responsible persons will be given an opportunity to comment on any developed proposal that a new WAMTC group be formed. The PBPA will then make a decision about whether a new group for WAMTC purposes should be formed among F1 drugs, or possibly make a recommendation to the Minister that a new therapeutic group be formed among F2 drugs. If the Minister indicates agreement to the formation of a new therapeutic group, those drugs automatically undergo WAMTC review.

Once a new WAMTC group has been formed, it is reviewed annually at the meeting where the PBPA deals with prices for drugs within its ATC classification.

ATTACHMENT E
WAMTC PROCESS – ANNUAL REVIEW

STEP 1a:

Competitive process for selecting dosage data source, or request from responsible person to change dosage data source 14 weeks before PBPA meeting

STEP 1b:

Responsible person notification and request for updated dosage data 10 weeks before PBPA meeting

STEP 2:

Dosage data submission by responsible persons due 8 weeks before PBPA meeting

STEP 3:

Raw data treatment and initial WAMTC calculation by PBPA Secretariat

STEP 4:

Request for price proposals 6 weeks before PBPA meeting

STEP 5:

Price proposals deadline 4 weeks before PBPA meeting

STEP 6:

WAMTC calculation using price proposals

STEP 7:

PBPA agenda paper preparation 2 weeks before PBPA meeting

STEP 8:

Notify responsible persons of PBPA outcome and invite final pricing confirmation

STEP 9:

Price changes for next appropriate PBS Schedule cut-off approximately 4 weeks after PBPA meeting

ATTACHMENT F
DATA SELECTION CRITERIA

Criteria for data selection

There are no straightforward ways of routinely deciding which set of sample dosage data is better or best in a given situation. It is very unlikely that, from a range of dosage data sources, there will be one standout candidate while the others all exhibit deficiencies against all or most important criteria. Rather, relative performance in a number of areas will need to be weighed up as there need not be one source that is superior across all relevant factors.

The WAMTC process involves realigning sample dosage data to reflect the relativities observed between formulations and/or strengths of drugs in combined Medicare Australia script numbers and DUSC under co-payment script estimates, and estimating the average cost per patient to the Australian Government of a month's treatment on this basis.

While sample dosage data are usually available only for GPs and each authority script is counted as "1" by Medicare Australia, these will often not have particularly important effects on estimates of the relative treatment costs for different drugs. In the absence of evidence to the contrary, the primary criteria for assessing the relative merits of different data sources can be boiled down to:

- how close together are the adjusted and unadjusted WAMTC estimates?
- how well do the dosage data reflect actual usage patterns for each drug?
- what other signs there are of one source better reflecting known conditions?

More detail about ways in which the relative merits of different data sources ought to be measured against these criteria are set out below. The assessment goes through two distinct phases:

- are there grounds for doubt about the overall reliability of one or more samples? (in which case the eligible field can be reduced)
- how well do the sample relativities appear to match the population estimates? (in which case measurement in terms of estimated standard deviations provides an appropriate normalisation)

Medicare Australia and under co-payment script relativities for different strengths critical

The WAMTC methodology involves realignment of sample dosage information at different strengths of a drug to reflect overall script relativities at those strengths. The extent to which the adjusted WAMTC departs from the unadjusted WAMTC will therefore be an important indication as to which sample is better or best.

The situation is somewhat complicated by the facts that:

- Medicare Australia processed script volumes and DUSC estimates of under co-payment script volumes are based on prescriptions written by all practitioners; and
- sample dosage data currently available are based on GP prescribing behaviour.

Consequently some instances where dosage sample strengths of a drug have different relativities from those of the corresponding combined Medicare Australia and DUSC global data might be partly or largely explained by knowledge that specialists or other practitioners are likely to have different prescribing patterns from GPs. It cannot just be assumed that discrepancies automatically reflect on the likely quality of the sample from which they arise.

Where there is evidence that observed differences can be ascribed in large part to failure to capture prescribing patterns of practitioners who are not GPs, there are several possibilities for making adjustments. For instance, there may be some empirical data that allow a range of distinct behaviours for these other groups of practitioners to be portrayed, and make feasible a WAMTC modification based on a weighted average of GP and remaining contributions. In these circumstances, the results obtained should be compared with those which establish the proportion of the Medicare Australia script volumes generated by prescribers who are GPs.

The comparison might best rely on the respective levels of departure from the indicated Medicare Australia + DUSC strength relativities and/or the impacts on WAMTC estimates once the WAMTC calculator's adjustment for global script strength relativities is made. Generally, the more that a WAMTC estimate changes in the adjustment process arising from alignment with Medicare Australia + DUSC relativities, the more a question mark is thrown over the representativeness of the sample data.

In considering the best measure through which to form these judgements, it is important to appreciate that the WAMTC methodology generates a 95% confidence interval around the adjusted WAMTC estimate and essentially bases pairwise comparisons of drug costs on this information. Therefore if the corresponding unadjusted WAMTC lies outside such a confidence interval for any drug, this is an indication that the sample data may not be representative.

In such cases, the scaled-back projected sample numbers (which appear as 'No. of observations in sample' after the unprojected and projected sample frequencies have been entered) would not be accepted as very consistent with the overall Medicare Australia + DUSC script volumes because of the inequality in respective WAMTCs. This in turn would cast doubt over the representativeness of the observed sample of prescribing behaviour. How many standard deviations the unadjusted WAMTC is away from the adjusted WAMTC will consequently be a very good indicator of how appropriate a particular data source is for these calculations; it is certainly a more sophisticated and robust measure than any comparison built around just percentage variation.

Sample size and precision

Larger samples will tend to pick up a wider range of dosages at a particular strength and appear to be more complete because there are no evident gaps. In addition, they will have lower relative standard errors, and therefore be more likely to meet the "25% or less" criterion that the Australian Bureau of Statistics uses as its primary benchmark for estimates to be seen as having sufficient reliability for most purposes, and to publish them.

If different sources of dosage data cannot be greatly separated through consideration of characteristics associated with the representativeness of prescribing patterns, available sample size becomes particularly important as the level of precision of the WAMTC estimates improves with sample size. This is reflected in the extent of the 95% confidence interval for a drug.

However, sample size alone is not a sufficient criterion if the patterns of prescribing picked up in the sample are more out of line with global script volume relativities than the prescribing patterns described in other smaller dosage samples that have been submitted for a WAMTC group.

Justification for departures from established sampling methodologies

Sampling should normally closely reflect actual usage patterns. Otherwise, greater importance is ascribed to certain drugs and lesser to others, without any obvious justification or methodological gain.

In some circumstances, a degree of stratification may be appropriate if it allows inferences to be drawn about more drugs. However, if this is not carried out carefully, the result may be an upgrading of reliability about what is a relatively small part of overall usage. This may be negated by the unnecessary loss of precision in estimates for the drugs that have most frequent usage.

The onus is on responsible persons to demonstrate the net gain in reliability where a sampling methodology results, for instance, in two-thirds of the anticipated population being compressed into just one-third of the sample.

Considerations of basic reliability and completeness

There are a number of general considerations that can be brought to bear in assessing the overall quality of available sample data before seeking to align it with what is (more or less) known about the entire population. If there are no grounds for questioning the reliability of a data source which generally has adjusted and unadjusted WAMTCs closer together, there is no need to systematically present evidence on the type of characteristics mentioned below. These are set out for those cases where more than one data source is evenly matched in relation to WAMTC distances.

Large proportions of recorded data incapable of being used lead to uncertainty about

whether population characteristics are being captured particularly well. For instance, if the proportion of unusable data because medicine strengths, dosage on each occasion or daily repetition is not specified remains beyond 10 per cent, it will not be certain that the remaining data reflect actual overall patterns. It may instead be affected by a tendency of prescribers to 'omit the obvious' in recording. This will result in under-representation of common dosage regimens at particular strengths.

Where there are fairly high levels of data wastage in all sources, relative amounts (for instance 5% against 10% for various individual drugs) may be an indicator of one source's better quality. However, differences need not manifest themselves uniformly in favour of a particular source.

A lesser criterion of this general nature is the ability to detect and reject implausible recordings and retain confidence about the understanding and treatment of outliers. If such occurrences are infrequent, apparent oddities may be more a reflection of the time available to generate and present a data extract and the thoroughness applied in cleansing the data. The presence of such outliers will not necessarily be a sign that the overall sample is more or less representative of population patterns, but, taken with other matters, may throw into greater doubt the demographic adjustment processes that are applied and whether they succeed in producing data reflecting national prescribing patterns.

Low frequencies

While dosages are typically concentrated on a small number of regimens, the recorded incidence of the ones with low frequencies may sometimes provide some useful guidance about how representative the sample appears to be. For instance, where two or more drugs are prescribed infrequently but not in negligible quantities, the question arises of whether the sample captures their overall relativity over the period in question. This may be complicated by ongoing trends towards greater use of some individual drugs.

More widely, there may be drugs that appear to be consistently missing or greatly under-represented in the sample dosage data and/or others that are consistently over-represented relative to overall Medicare Australia + DUSC patterns. If so, in the absence of other plausible explanations, this may be a sign that the sample has picked up too much of a particular prescribing pattern among its small numbers, or that unusual circumstances in which a drug tends to be prescribed are not picked up very well among the consultations sampled in the prescriber population.

Where particular dosages typically occur more than just once or twice, tracking their relativity to the dominant dosage at that strength over time may give an indication of the extent to which there is apparently a consistent relationship. Major unexpected fluctuations are likely to be indicative of atypical patterns occasionally being reflected in a particular sample.

If particular dosages tend to occur just once or twice or not at all, such prescriptions rarely occur and not too much can be inferred from whether or not a non-zero sample frequency is

present in a particular time period. When considered over a number of different periods, whether or not the same broad pattern recurs may give a feel for underlying stability in a particular array of small frequencies, including the possibility that each of its components reflects a phenomenon with Poisson or other broadly predictable experience.

Summary

In summary:

- evidence available from the differences between the unadjusted and adjusted WAMTCs;
- systematic consideration of general sample characteristics; and
- the way in which low dosage frequencies are captured;

will usually give a good indication of whether a particular sample departs to an important degree from capturing overall known prescriber behaviour.

If a particular dosage source comes out well under this type of close scrutiny and achieves the greatest precision because it has noticeably larger sample numbers than those of its most pressing competitor(s), it will be the best choice for that WAMTC group. Otherwise all the pros and cons need to be carefully weighed, with special reference to how far apart are the unadjusted and adjusted WAMTCs.

Three-year cycle

Beyond ordinary sample variation inherent in any dosage data source, a further source of variability is introduced if there is constant swapping among data sources.

The WAMTC process needs to find the most appropriate balance between giving responsible persons the greater level of certainty associated with continuing use of a particular suitable data source for a period of time, and being open to recognise deficiencies or improvements when they arise.

The approach being taken is to allow responsible persons to put forward their preferred dosage data sources once every three years, and to build in a fair presumption that the source selected for the review on the basis of the objective criteria set out above will remain in use for the next three years. Specifically:

- the PBPA has determined that the dosage data source at an ad hoc review will be the same as that used at the previous annual WAMTC review for that group (in the event that no sample dosage data are forthcoming from responsible persons, the PBPA Secretariat will obtain BEACH data or, dosage data from another provider if required);
- after a data source has been chosen in a potentially-competitive environment, it will remain in force for all annual and ad hoc reviews for that group for three years unless a responsible person has demonstrated its deficiencies and proposed a better alternative at least 14 weeks before a meeting at which the PBPA conducts an annual WAMTC

review;

- where more than one responsible person demonstrates the deficiencies in a current dosage data source and proposes an improvement without agreeing on the new source, the criteria set out above for determining which source to use in a particular situation will be applied to the period over which the review is to be undertaken, and the selection made on these grounds by the PBPA Secretariat after responsible persons have had an opportunity to comment on the relative merits of the new data sources that have been advanced.

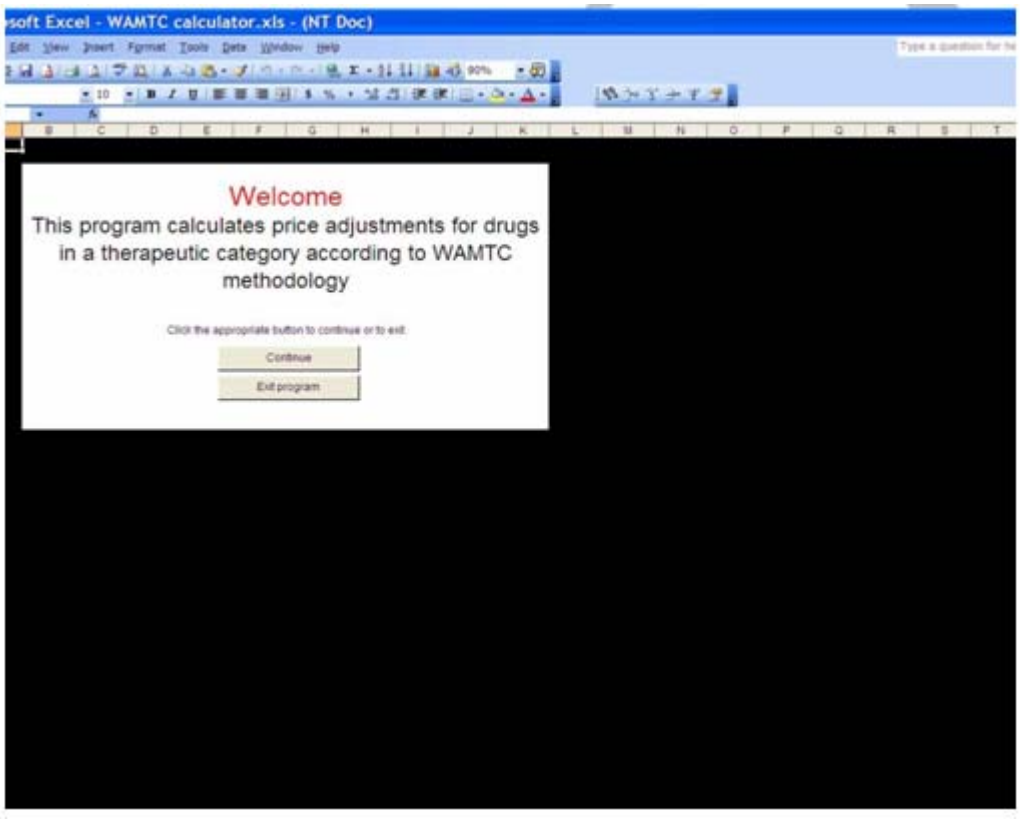
In order to establish that the default dosage data source should no longer apply, a responsible person will need to demonstrate the following over a recent four-quarter period:

- the adjusted and unadjusted WAMTCs for a majority of drugs in the group with multiple strengths and/or formulations are at least two estimated adjusted WAMTC standard deviations apart;
- for a majority of such drugs with distant WAMTCs, the proposed replacement data source has adjusted and unadjusted WAMTCs closer together; and
- for a majority of the drugs in the group with multiple strengths and/or formulations, the adjusted and unadjusted WAMTCs arising from the proposed replacement data source are closer together in terms of the number of standard deviations.

ATTACHMENT G
USING THE WAMTC CALCULATOR – FROM START TO FINISH

When you open *wamtc.xls* you have:

- on the *Welcome* page a **Continue** button through which you are able to generate one spreadsheet for each drug in your group;
- a seemingly blank *Summary Sheet* page on which various headings have been entered, along with a number of formulae that are activated once calculated values have been transferred from the individual drug worksheets;
- *Adjusted WAMTC chart* and *Unadjusted WAMTC chart* pages on which WAMTC point estimates and confidence intervals will be plotted after the calculations have been set in train by a macro;
- a *Question sheet* page on which will automatically appear (and be visible if you remove the black colouring) the names that you give to the various drugs.



There is also elaborate coding for several macros that is accessible to you through clicking on **Tools – Macro - Visual Basic Editor**. However if you wish to explore this level of detail, it is advisable to create a separate copy of the calculator in case you inadvertently save modifications of the original.

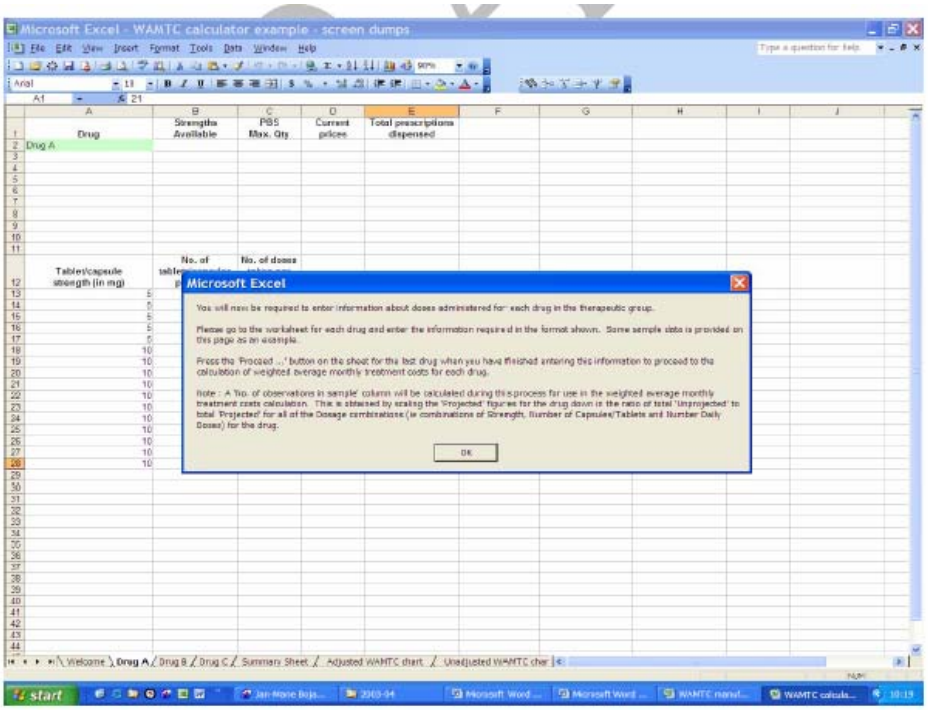
To set up your series of calculations for a particular WAMTC group you:

- press the **Continue** button;
- type the name you wish to give the group in the first prompt and press **Enter** (this name will automatically be placed at the top of the *Summary Sheet* page);
- type how many drugs there are in the group (you should enter an integer between 2 and 15, the maximum number of drugs the calculator can handle);
- type the name of each of the drugs.

When the last of the names has been entered, a message box appears to alert you that only numbers need be entered in the various columns. After you click **OK**, the calculator automatically sets up a separate page for each drug and enters its name in various spots on the four sheets that were originally visible in addition to the *Welcome* page.

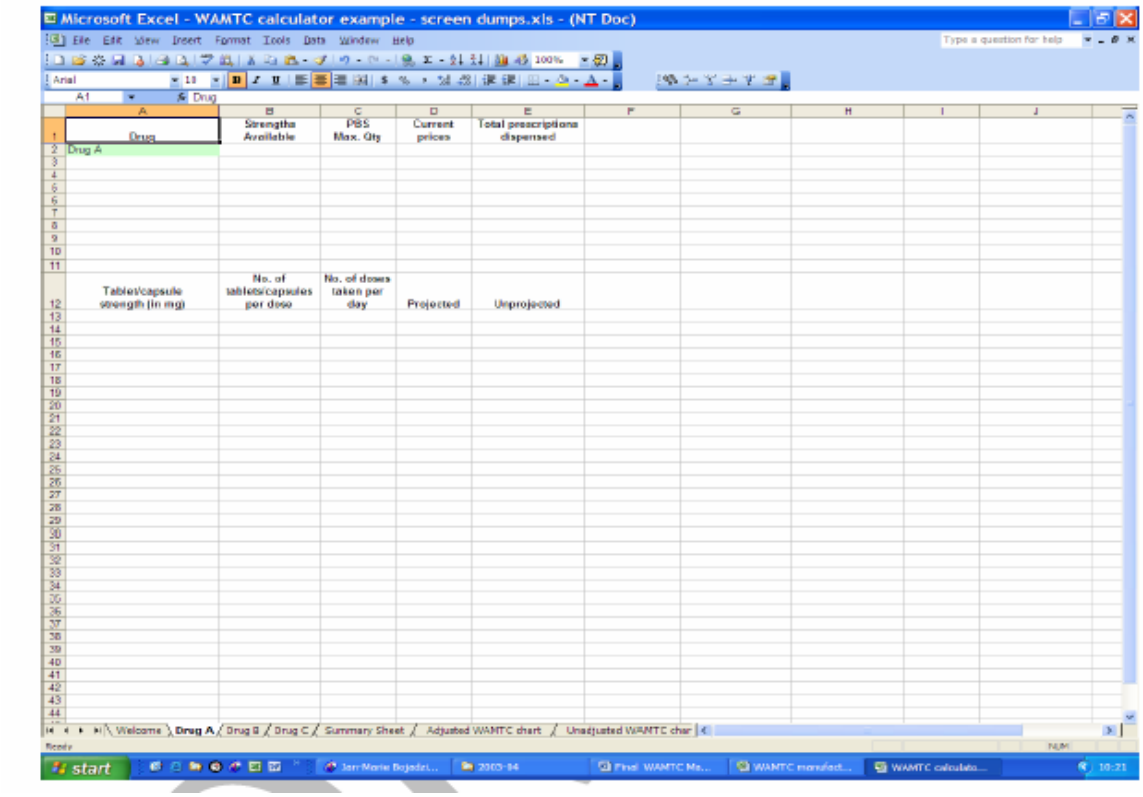
Note: it is preferable to enter the names exactly as you will want to see them appear on the calculator spreadsheets thereafter. You will only need to enter these particulars once if you save a pre-calculation copy of these spreadsheets as recommended later – in future, you will be able to amend usage, price and dosage particulars without re-entering all these details. If you make a mistake when entering the names, and are particular about their appearance on the *Summary Sheet* and other worksheets and the two charts, it is quicker to start from scratch rather than try to modify what has been built up.

A message box comes up advising you that you are about to enter various pricing, usage and dosage particulars for each drug under column headings that already appear on each individual drug page, and that a **No. of observations in sample** column will be generated automatically from the entries in the **Projected** and **Unprojected** columns:



- you need to click the **OK** button to move on from here;

- on clicking, you are taken to the first drug page where some dummy numbers automatically appear under the second set of column headings and can immediately be deleted;
- the same sets of headings appear on each drug page, and the drug names are positioned in appropriate cells on each page and entered as worksheet names.



At the top of each drug page, you will find the four column headings:

Strengths Available	**PBS Max Qty**	**Current prices**	**Total prescriptions dispensed**

- the entries for the first three columns are found in the latest *Schedule of Pharmaceutical Benefits* and can be copied elsewhere for future pasting and minimal effort when amending to create variations or updates;
- for a given drug, each different strength will have a separate PBS item code in the left-hand margin and a list of the different brands available in the **Proprietary Name and Manufacturer** entries in the two rightmost columns on each page – later, it will be vitally important to combine dosage data for the different brand names given as well as those appearing under any more general name(s) for that particular strength;
- you enter only the numerals corresponding to **Manner of Administration and Form** for the strengths, together with those under **Max Qty** and generally those under

Dispensed Price for Max. Qty;

- however, brand or therapeutic group premiums or special patient contributions are disregarded when entering prices, so if there is a non-zero entry in the **Premium** column in the *Schedule*, this must be subtracted from what appears in the adjacent **Dispensed Price for Max. Qty** column before it can become a **Current prices** entry – some caution needs to be exercised where for drugs such as lercanidipine hydrochloride, the therapeutic group premium appears for the listing in ordinary circumstances but not when an Authority is required (the volumes for both the ordinary and Authority listings are combined, at the price established by subtracting the premium for the ordinary PBS item);
- liquid forms of drugs are included in WAMTC calculations and some care will usually be required to properly calibrate quantities;
- where the same strength is available in both tablet and capsule form with different PBS item codes, it is advisable to differentiate these by adding say 0.000001 to the second to keep them as separate entities without affecting calculations materially – without a separation of this kind, the calculator is unable to make full use of all the collated Medicare Australia and Drug Utilisation Sub-Committee (DUSC) information and in any case stalls when it comes to a repeated strength (as the actual strength does not enter the dosage-and-price calculations, it does not matter what new marker is used to indicate a difference in the PBS items involved);
- the only alternative where there is no variation in price or pack size is to combine prescription and later dosage numbers for each of the strengths – as separate Medicare Australia volumes are available for each item, this pooling will in general have an impact on both the WAMTC point and variance estimates, making the latter larger than necessary in view of the additional available information that is not being used;
- the entries for **Total prescriptions dispensed** are the sum of Medicare Australia records for a particular strength over a twelve-month period (available at https://www.medicareaustralia.gov.au/statistics/dyn_pbs/forms/pbs_tab1.shtml according to the different PBS item numbers) and DUSC estimates from Pharmacy Guild sample data of the corresponding numbers over the same period of any prescriptions to general patients costing less than the maximum contribution rate or co-payment (and therefore not being captured in Medicare Australia data because the Australian Government doesn't make a contribution to the cost);
- Medicare Australia quarterly data tend to be available within a few weeks of the end of a quarter, while Pharmacy Guild sample data from DUSC are usually available within three months of the end of a quarter;
- in the lead-up to WAMTC methodology calculations and price adjustments, the information about **Total prescriptions dispensed** will be supplied electronically by the PBPA Secretariat to correspond with the most recently available four quarters' sample dosage data.

In row 12 on each drug page, you will find the columns:

Tablet/capsule strength (in mg)	**No. of tablets/capsules per dose**	**No. of doses taken per day**	**Projected**	**Unprojected**

The material to be entered here will best be calculated elsewhere as a block of data ready for copying with an **Edit – Paste Special – Paste Values** command.

- **Unprojected** column entries are the raw sample numbers for particular daily dosages of a drug and indicate a level of inherent variability that cannot readily be circumvented;
- **Projected** column entries will usually be the result of demographic and other adjustments made to raw sample numbers by data suppliers, followed by factoring up to estimated national levels;
- from these two sets of entries, the calculator will generate another column called **No. of observations in sample**, scaling back the **Projected** column entries in the ratio of the sum of all **Unprojected** column entries to the sum of all **Projected** column entries;
- what is achieved is essentially a demographic correction for known sample characteristics, within the constraint that the total of these **No. of observations in sample** entries must match the total of the raw sample numbers (and therefore reflect the inherent variability in these data in the WAMTC variance estimates);
- in the event that a data source does not give separate projected or corrected entries, repeat the same column here for both the **Unprojected** and **Projected** entries - the **No. of observations in sample** column will then also be identical to these.

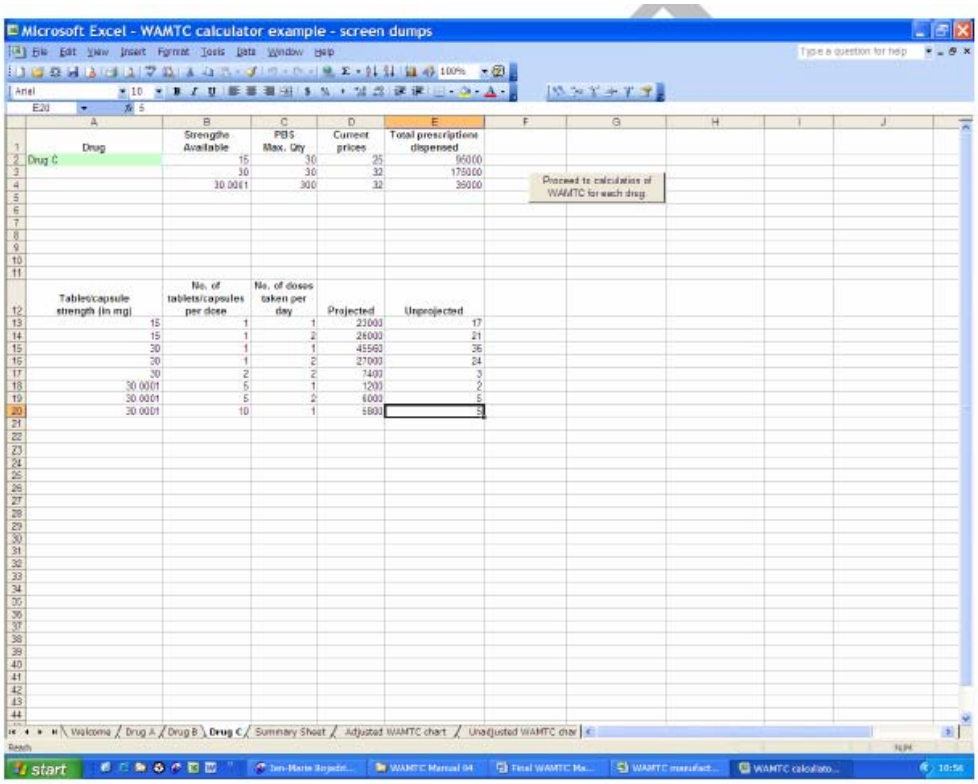
Unless great care is taken in combining all the contributors to a particular strand of dosage data, errors in the WAMTC calculations will be inevitable:

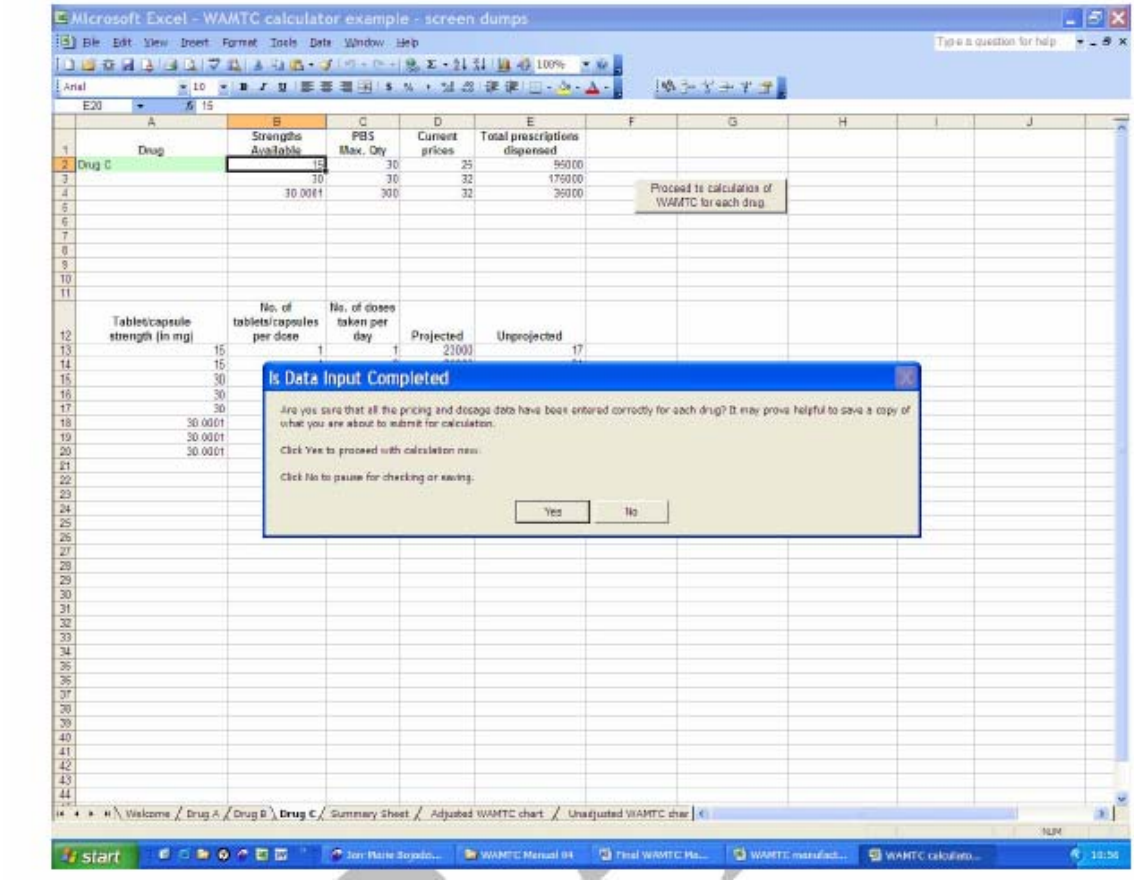
- the first step is to identify all the names in the dosage data source under which a particular strength (or PBS item code) can appear, bearing in mind circumstances where this may not be as straightforward as just identifying the different possible brand names – it may then be possible to add various row entries that are presented in an Excel format to arrive at the dosage frequencies desired and transpose these numbers into the required format through an **Edit -Paste special – Values & Transpose** command;
- errors are less likely if non-zero frequencies are sought systematically as daily dosages at a particular strength are increased – for instance start by looking for non-zero frequencies corresponding to 5 mg strength being taken at a dosage of 0.5 tablet a day, then check the same strength at dosages of 1 tablet a day and 1.5 tablets a day and so on, before moving to see whether 0.5 tablet a day for 10 mg strength features at all;
- if row-addition formulae have been used to generate the **Projected** column dosage entries from projected data, copying the cells with these formulae and pasting them in exactly the same spot relative to the unprojected data should automatically generate the corresponding **Unprojected** column entries;
- • the use of a pivot table approach is likely to minimise both potential for inadvertent error and the time required to summarise the data for entry into the WAMTC calculator – it relies on the construction of additional columns to classify dosage data in a matrix that makes cross-tabulation straightforward;
- 'not specified' entries, either as dosages for particular strengths or where the strength itself is uncertain, are disregarded (rather than distributed in one way or another) - if they continue at relatively high levels for any length of time, a concerted approach to

get data suppliers to tackle the problem may be necessary.

Close attention will be necessary if particular phenomena are observed:

- in some cases, especially with drugs with very low numbers of prescriptions, there may only be a single dosage recorded in the sample – in that case, without variation the WAMTC variance will be zero, "#DIV/0!" will appear in various calculated cells and the particular drug cannot become the benchmark;
- if the total number of **Unprojected** scripts at all strengths for a particular drug is less than 65, there is sufficient uncertainty in the WAMTC variance for agreement to have been reached that the particular drug cannot become the benchmark;
- unless a responsible person advises that they are about to be withdrawn from the market, all drugs for which sufficient sample scripts are available become eligible to be the benchmark drug when price proposals are requested as these only involve cost to the Australian Government - brand premiums, and TGPs cannot be considered until the benchmark drug and lowest prices at each strength or formulation of a drug are known;
- in these circumstances, it is possible that there will be a need to carry out a second WAMTC calculation because the drug originally identified as the benchmark on the standard criteria applied is ineligible for one of the above reasons – this is also why, when you click the **Proceed to calculation of WAMTC for each drug** button on the final drug page, a message box appears asking whether you are satisfied all the data have been entered correctly and indicating that it may prove useful to save the Excel file at this pre-calculation stage.

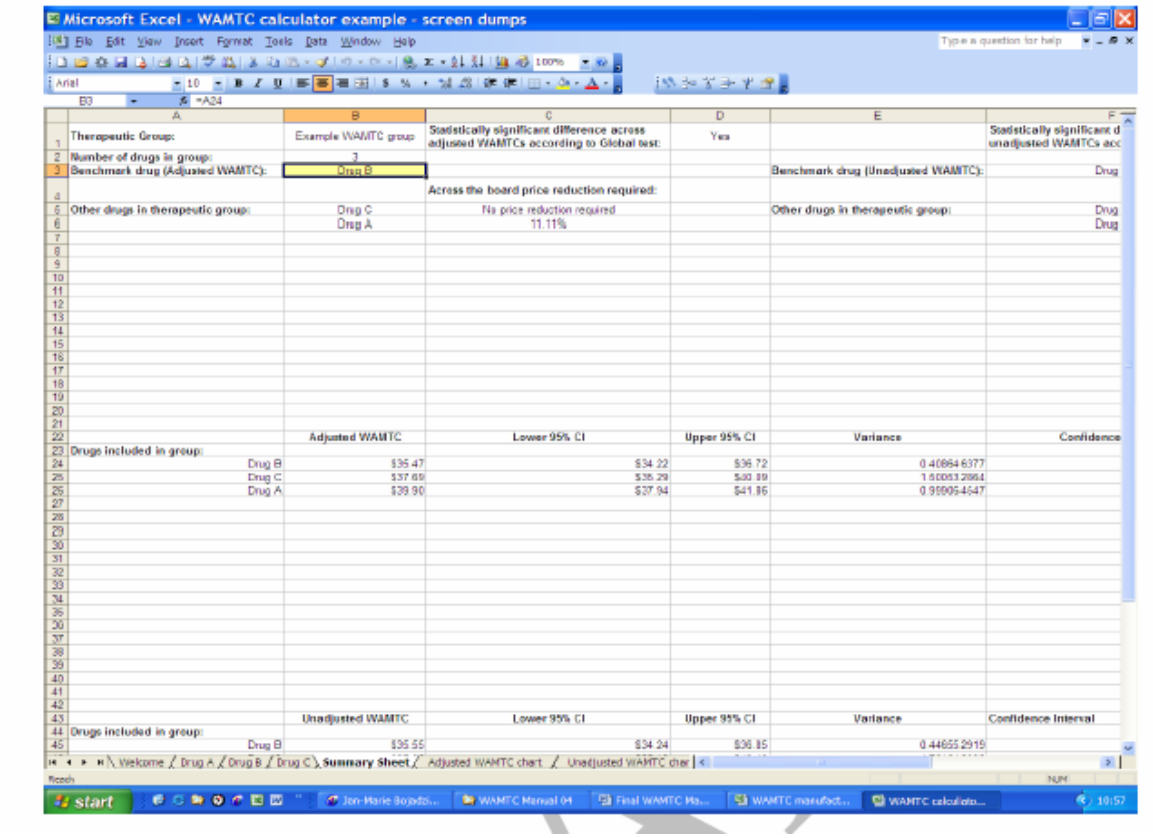




All drugs within a WAMTC grouping are included in the original WAMTC calculation as it is quite possible that the one designated as the benchmark will be eligible for that purpose, and no reason to automatically suppose otherwise:

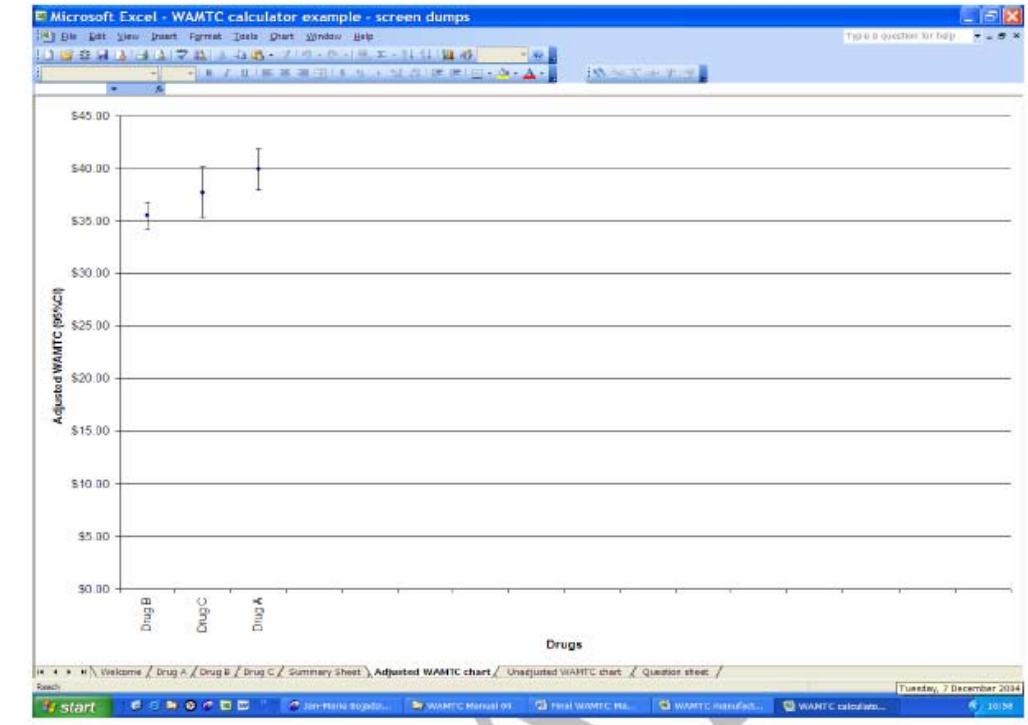
- if not, a second calculation is undertaken after the ineligible drug's particulars have been removed from the calculation – because of how a macro and various pre-entered formulae in cells have interacted, this is not as simple as deleting the worksheet corresponding to the ineligible drug;
- if the file particulars have been saved just prior to the enabling of the major WAMTC calculation macro, the discovery of an ineligible drug initially proposed as the benchmark does not delay the recalculation for long - the data particulars for each of the remaining drugs can be copied onto the appropriate pages in a revised Excel file generated by opening the blank calculator and re-entering the drug names except the one that is ineligible.

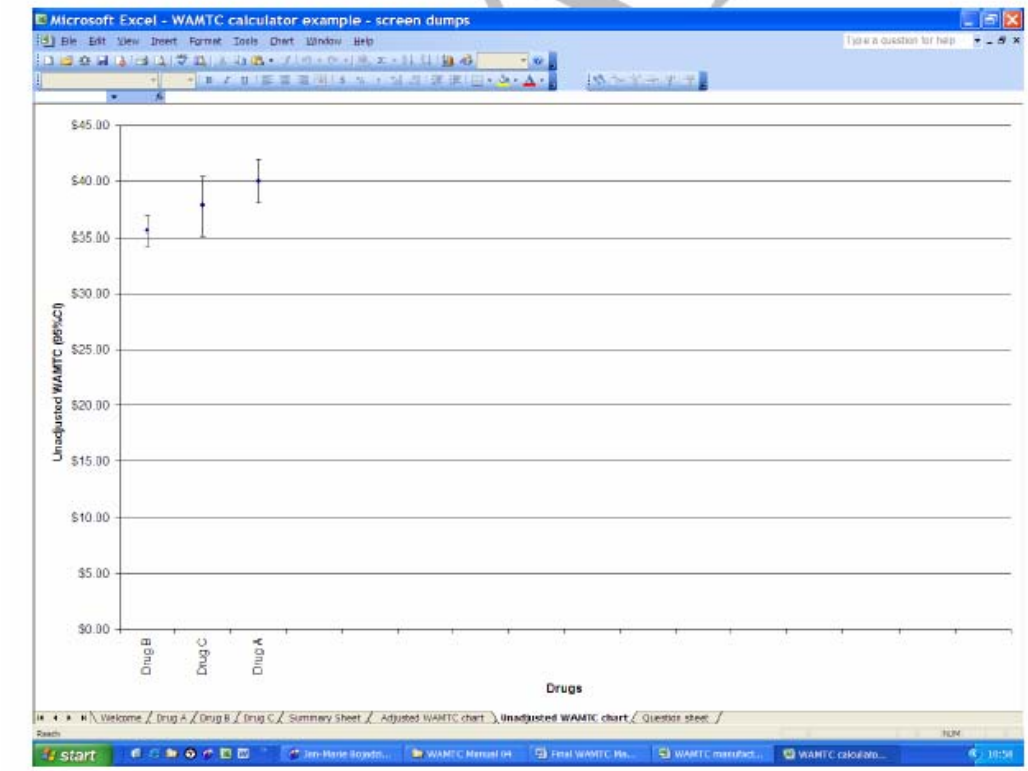
Once the calculator button has been activated, the most substantial of the macros carries out a host of calculations on each drug page and transfers key particulars to the *Summary Sheet* page and the two charts:



- the button itself immediately goes into hiding so that no-one will be tempted to discover what happens if it is clicked a second or third time;
- both **adjusted** and **unadjusted WAMTC** particulars (point estimate, estimated variance and 95% confidence interval) are summarised in blocks G14:I16 and K14:M16 on each drug worksheet;
- **unadjusted WAMTC** particulars are generated on the basis of just the entries in the **No. of observations in sample** column – there is no a priori guarantee that the sample data are particularly good or that the WAMTC estimate is an unbiased one;
- the **adjusted WAMTC** particulars involve the use of the known total script data at different strength levels (Medicare Australia recorded volumes plus DUSC below co-payment estimated numbers generated from the Pharmacy Guild sample) to realign the way in which the WAMTC and its variance are estimated;
- the incorporation of the additional information on total script proportions at different strengths (relying on calculations in cells E2:I2 and below on each drug worksheet) will cause a reduction in the estimate of WAMTC variance unless a drug has a single strength (in which case adjusted and unadjusted estimates are clearly the same);
- the WAMTC point estimates themselves are not particularly complicated – any noticeable differences between the unadjusted and adjusted ones are an indicator that the sample is not particularly representative of the relative frequencies with which individual strengths of a drug are prescribed;

charts summarising the adjusted and unadjusted WAMTCs for each drug (with their 95% confidence intervals) are also produced on the *Adjusted WAMTC chart* and *Unadjusted WAMTC chart* worksheets.





ATTACHMENT H
PRICE PROPOSAL TEMPLATE

The price response is the cost to the Australian government and is the amount eligible for entry into the WAMTC calculator

Date: --/--/--

WAMTC Group

Responsible person

Drug name(s)

1. Drug name	2. Formulation, Strength and Pack Size	3. Price response [i]-[v]	4. Default entry if no response received [vi]	5. Contingent price response [vii]-[viii]
Drug A	Tablet, 10mg, 30		current DPMQ less any brand premium or TGP	
	Tablet, 20mg, 30		current DPMQ less any brand premium or TGP	
Drug B	Tablet, 20mg, 30		current DPMQ less any brand premium or TGP	
	Tablet, 40mg, 30		current DPMQ less any brand premium or TGP	
	Tablet slow release, 40mg , 30		current DPMQ less any brand premium or TGP	

Price response

(i) Options in relation to brand premiums (BPs) and therapeutic group premiums (TGPs) will only be known after the benchmark drug and lowest prices offered at each formulation and strength of every drug have been established.

(ii) From the price responses received (including default entries where applicable), at each formulation and strength of every drug the lowest price will be chosen for entry into the WAMTC review calculation.

(iii)This is an offer in the sense that if you submit the lowest price for a particular formulation and strength and your drug is the benchmark or has a WAMTC that is statistically equal to the benchmark WAMTC, the drug must be available from at least one responsible person at that price after the review.

(iv) If a drug's WAMTC is significantly higher than that of the benchmark drug, a reduction in the WAMTC will be required.

Where there are multiple responsible persons of the drug concerned, any reductions already offered will be disregarded when assessing the level of across-the-board reductions that is necessary.

(v) If you are seeking an increase in the cost to the Australian government for any strength/formulation (i.e. your price response is greater than the default entry), a PB11 (b) form must be submitted along with your response.

Default response

(vi) If no response is received, you will be assumed to propose the current DPMQs less any premiums previously imposed.

Contingent price response

(vii) This is an alternative price response to be used in situations where the PBPA needs to consider a submission (eg price increase at one or more formulations and strengths, partial exemption or exclusion) and the responsible person does not wish to revert to a default of the current DPMQs less any premiums previously imposed, if unsuccessful. For responsible persons who did not initiate a submission, to vary the standard WAMTC calculation, the contingent price response is for situations where such a submission is accepted. Should a submission other than a request for a price increase be *partially* accepted, you will be contacted to see whether you wish to vary your price response.

(viii) Any contingent price response received in situations where the PBPA does not first need to consider a submission in relation to the particular drug will be disregarded.

ATTACHMENT I
WAMTC PROCESS – AD HOC REVIEW

STEP 1:

Responsible person requests price reduction and if possible supplies latest dosage data from the same source as preceding annual review
10 weeks before PBPA meeting

Notification of trigger for ad hoc review and request for dosage data from other responsible persons
(if not provided with price reduction request)
10 weeks before PBPA meeting

STEP 2:

Dosage data submission by responsible persons due
8 weeks before PBPA meeting

STEP 3:

Raw data management and initial WAMTC calculation by PBPA Secretariat

Determine need for full ad hoc review
Does price reduction result in the global test showing a difference in the WAMTCs of the drugs in the group?
If no difference found, review stops.

STEP 4:

Request for price proposals

6 weeks before PBPA meeting

STEP 5:

Price proposals deadline

4 weeks before PBPA meeting

STEP 6:

WAMTC calculation using price proposals

STEP 7:

PBPA agenda paper preparation
2 weeks before PBPA meeting

STEP 8:

Notify responsible persons of PBPA outcome
and
invite final pricing confirmation

STEP 9:

Price changes for next appropriate PBS schedule

cut-off approximately 4 weeks after PBPA meeting

ATTACHMENT J
HONING IN ON A WAMTC NOT SIGNIFICANTLY GREATER THAN THAT OF THE BENCHMARK DRUG

As outlined in ***Section 4***, responsible persons are provided with a pre-calculation version of the WAMTC calculator for their group by the PBPA Secretariat, and are able to run different scenarios through the calculator to determine the best strategy for price proposals (remember to save a pre-calculation version with the original data, so you do not have to set up a new calculator each time).

Where the current WAMTC calculation shows a drug to have a WAMTC statistically significantly greater than that of the benchmark drug, price proposals for that drug should normally involve reductions in order to achieve a WAMTC not statistically different from that of the benchmark drug. The final benchmark drug and its WAMTC will, of course, only be known after price proposals for the group are received. However, should the current benchmark WAMTC remain, and a responsible person not propose to reduce prices, or their price proposal not result in the drug's WAMTC being statistically equal to that of the benchmark drug, the responsible person will be required to reduce to the point estimate of the benchmark WAMTC upon completion of the review.

The percentage across-the-board price reductions required for a drug to match the point estimate of the benchmark drug's WAMTC will be found on the *Summary Sheet* worksheet in the calculator. The opportunity to submit price proposals is a chance to submit prices that result in a WAMTC not significantly different from that of the benchmark drug. Thus, responsible persons may be able to avoid the full across-the-board percentage price reductions required to match the point estimate for the benchmark drug.

The across-the-board price reductions indicated in the *Summary Sheet* worksheet are associated with the z-statistics arising from pairwise tests, in column M. Where a drug has a WAMTC significantly greater than that of the benchmark drug, the z-statistic for this drug will show a value greater than 1.96 (the critical value). The crossover from a WAMTC being significantly greater than that of the benchmark drug to not being statistically distinguishable occurs at a value just below 1.96. The z-score arises from taking the difference between two WAMTCs (each of which can be assumed to be normally distributed) and dividing by the square root of the sum of their two estimated variances. Where price reductions are offered, both the WAMTC of the drug involved and its variance will decrease.

For illustrative purposes, let's say we need to take a z-score from 15.20 to just under 1.96. For this example, let's also say that the across-the-board reduction required to match the point estimate of the benchmark is indicated to be 6.48% (this produces a z-score of 0). By offering a bit more (to take into account of the decrease in the denominator of the z-score as the drug's WAMTC variance decreases) than (15.20 – 1.96)/15.20 * 6.48% we should be rather close to achieving a z-statistic just under 1.96. This is just over 5.64%. It might be reasonable to try a reduction of 5.66%.

To achieve this across-the-board, multiply each current value (DPMQ less any premiums for each formulation and strength) by 0.9434 and enter these new prices into the calculator. It may take a few tries before the percentage reduction gives a z-statistic just under 1.96. You can try adjusting the different strengths by one cent to see how the results are affected, and calibrate on that basis. As a rough guide, a one cent change at each strength often has a z-score effect of around 0.05 in the region near the crossover value.

Of course, there are still the strategic questions of whether one strength is more important to a responsible person than the others, and how much of a buffer to leave against possible surprise developments.

Note:

Remember to re-run the calculator with the new prices each time. Do not simply try to adjust the values in the calculated worksheets or summary sheet.

This technique for honing in on a WAMTC not statistically significantly greater than that of the benchmark is based on certain assumptions about the movement in prices of the other drugs in the group. This technique does not guarantee a further price reduction will not be required for the drug, should the benchmark drug's WAMTC decrease after price proposals are received.