Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

AWMSG Appraisal Process: frequently asked questions

These questions and answers should be read in conjunction with the following documents which can be found under the All Appraisal Documents section on the AWMSG website:

- AWMSG appraisal process flowcharts:
  - Appraisal principles and process
  - Decision process for full, limited and licence extensions for paediatric use submissions
  - Appraisal process timeline (full and limited submissions)
  - Appraisal process timeline (licence extensions for paediatric use)
- AWMSG process for industry engagement
- AWMSG exclusion criteria
- Policy for appraising a medicine to treat a very rare disease
- Policy for appraising a medicine to treat a severe condition
- AWMSG guidance notes for completing Forms A, B & C
- Form A – initial submission
- Form B – full submission
- Form C – limited submission
- Guidelines for appraising medicines
- Independent Review (IR) Process
- Agreement between the Association of British Pharmaceutical Industry (ABPI) and the All Wales Therapeutics and Toxicology Centre (AWTTC) on guidelines for the release of company data into the public domain during an appraisal

This document aims to provide answers to frequently asked questions and has been separated by the following categories:

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General information

What is the remit of AWMSG in relation to appraisals?
AWMSG makes recommendations to Welsh Government in relation to the use of new medicines within NHS Wales. Initially the AWMSG appraisal process focused on high-cost medicines (i.e. those costing > £2,000 per patient per annum). In April 2007, Welsh Government increased AWMSG's capacity to review new medicines up to a total of 32 appraisals per year. These comprised of not only high-cost medicines, but also new cardiovascular, malignant disease and immunosuppressant medicines. In December 2009, Welsh Government announced that funding would be available from April 2010 for AWMSG to broaden its remit to appraise ALL new medicines not on the National Institute for Health and Care Excellence (NICE) work programme. The implementation date for the broadened process was 1 October 2010. To avoid duplication of effort, AWMSG would not **normally** consider undertaking an appraisal if NICE intends to publish guidance (as a single technology appraisal [STA] or multiple technology appraisal [MTA]) or highly specialised technologies [HST] evaluation) for the same medicine and indication(s) within 12 months of the date of marketing authorisation. AWMSG advice is interim to that of NICE, should NICE subsequently publish guidance as an STA, MTA or HST. NICE clinical guidelines are not mandatory within NHS Wales. In addition to new medicines receiving their first licence, new indications and formulations of previously licensed medicines can also be considered.

What is the remit of the All Wales Therapeutics and Toxicology Centre (AWTTC) in relation to appraisals?
AWTTC provides professional and administrative support to AWMSG. AWTTC critiques the information provided by the applicant company together with any other relevant publicly available information to produce the AWMSG Secretariat Assessment Report (ASAR) which is considered by the New Medicines Group (NMG) and AWMSG alongside other relevant documentation. In the case of licence extensions to medicines for paediatric use, when certain criteria are met, an AWTTC assessment report is considered by AWMSG.

What is the remit of the New Medicines Group (NMG) in relation to appraisals?
NMG is a subgroup of AWMSG which considers the clinical and cost-effectiveness of the medicine, based on written evidence from the applicant company, the AWMSG Secretariat Assessment Report (ASAR), views from clinical experts in the field and relevant patients/carers/patient organisations. NMG makes a preliminary recommendation to AWMSG in relation to each medicine undergoing appraisal. Up to ten NMG meetings are scheduled per year, which are held in private. NMG do not appraise licence extensions to medicines for paediatric use that meet certain criteria. If a submission meets the criteria for the licence extension for paediatric use process the medicine will then only be appraised by AWMSG.

Is the membership of AWMSG and New Medicines Group (NMG) public?
Yes, the membership of AWMSG and NMG is displayed on the AWMSG website.

Does AWMSG appraise a medicine if it has been appraised by the Scottish Medicines Consortium (SMC)?
Yes, if it meets AWMSG's criteria for appraisal; SMC's advice does not apply to NHS Wales.

What is the relationship between AWMSG appraisals and those of the National Institute for Health and Care Excellence (NICE)?
AWMSG takes into account the NICE future work programme when considering whether a medicine will be appraised. To avoid duplication of effort, AWMSG would not **normally** consider undertaking an appraisal if NICE guidance (single technology appraisal [STA] or multiple technology appraisal [MTA] or highly specialised technologies [HST] evaluation) for the same medicine and indication(s) is expected within 12 months of the date of marketing authorisation. AWMSG advice is interim to that of NICE, should NICE subsequently publish final technology appraisal advice or HST. NICE clinical guidelines are not mandatory within NHS Wales.

What if the National Institute for Health and Care Excellence (NICE) appraises a medicine but does not recommend its use on the grounds of lack of cost-effectiveness, but the medicine is available to patients living in England through alternative commissioning routes?
In January 2014 AWMSG adopted a new approach intended to address some of the issues relating to equity of access in relation to new medicines for patients in Wales. It will apply in circumstances when NICE does not recommend a medicine for use within the NHS on the grounds of cost-effectiveness and the medicine is subsequently funded within England through alternative national commissioning routes. An opportunity now exists for the applicant company to make an application for the medicine to be appraised by AWMSG. The application will be expected to include a Wales Patient Access Scheme (WPAS), but may also include additional information which may not have been submitted to NICE, or information specific to NHS Wales (perhaps highlighting a specific patient population or other societal benefit/s). It is important that any additional evidence showing added value or benefit to NHS Wales over and above that considered by NICE is clearly identified, highlighted, and reflects the context of an AWMSG appraisal which applies clinical and cost-effectiveness, in addition to a broad strategic, societal and patient perspective to its recommendations. It is also important that confirmation and full details of the alternative funding route within the NHS in England are provided.

What if the National Institute for Health and Care Excellence (NICE) appraises a medicine to treat cancer and recommends that it is only available to patients through the Cancer Drugs Fund?
NICE may recommend that a medicine to treat cancer is only available to patients through the Cancer Drugs Fund. This happens if NICE thinks the medicine is likely to meet the criteria for routine commissioning, but is uncertain about its benefits to patients and wants more data to be collected in the NHS or in clinical studies.

When a NICE technology appraisal recommends the use of a medicine or treatment, or other technology, for use through the Cancer Drugs Fund, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of NICE's final appraisal document or agreement of a managed access agreement by the NHS in Wales, whichever is the later.

The Cancer Drugs Fund is a source of funding for cancer medicines in England. The applicant company needs to agree a managed access agreement (MAA) with NHS England, and is encouraged to share the details with NHS Wales through the National Procurement Lead Pharmacist for Wales. Sometimes, the applicant company may need to agree an alternative MAA or commercial access agreement

(CAA) with NHS Wales, which offers equivalent value during the managed access period.

What communication links exist between the pharmaceutical industry and the All Wales Therapeutics and Toxicology Centre (AWTTC)?
Representatives from the pharmaceutical industry regularly meet with representatives from AWTTC to discuss general issues relating to the appraisal process. Individual pharmaceutical companies are encouraged to communicate regularly with AWTTC in relation to future or on-going appraisals. Enquiries should be directed to Mrs Ruth Lang, Head of Liaison & Administration by email awttc@wales.nhs.uk or by telephone on 029 218 26900.

How does the AWMSG appraisal process impact on individual prescribers?
Individual clinicians should take account of guidance issued by the National Institute for Health and Care Excellence (NICE) or AWMSG when exercising their clinical judgement, unless there is evidence to justify not doing so in the light of particular circumstances of an individual patient.

How are potential appraisals identified?
The onus for engagement lies with the applicant company to submit Form A. The All Wales Therapeutics and Toxicology Centre (AWTTC) 'horizon scanning process' also informs the AWMSG appraisal process. AWTTC identifies medicines expected to receive marketing authorisation within 18 months and may choose to refer the company to the AWMSG appraisal process.

What are the criteria for deciding whether a medicine undergoes an appraisal?
AWMSG appraises all new medicines that do not meet AWMSG's exclusion criteria. The decision as to whether a change in indication or formulation is 'significant' and requires appraisal is made by AWMSG on a case by case basis.

What if the criteria for appraisal by AWMSG are not met?
Within one month of receipt of Form A, the All Wales Therapeutics and Toxicology Centre (AWTTC) will confirm in writing (by email or letter) that appraisal by AWMSG is not required. Once marketing authorisation is granted, the AWMSG website will be updated to display the medicine details and the criteria under which it has been excluded from appraisal. If the application has been declined because it is on the National Institute for Health and Care Excellence (NICE) work programme, a link to the relevant NICE webpage is also included. The exclusion criteria are designed to provide broad guidance on products which fall outside the role and remit of AWMSG and where progression to formal appraisal is unlikely. In these circumstances health boards may consider whether individual products are appropriate for local formulary inclusion.

What approach is taken when a medicine has multiple indications?
In determining whether a medicine meets the criteria for appraisal, the All Wales Therapeutics and Toxicology Centre (AWTTC) will consider the whole licensed indication. In certain circumstances, a pragmatic approach may be adopted and separate appraisals may be undertaken if the licensed indication covers distinctly separate disease areas.

Can the applicant company request appraisal of a medicine for part of the licensed indication or in a particular patient population?
AWMSG appraise medicines for the full licensed indication(s) as detailed in the Summary of Product Characteristics (SPC). Supporting evidence for the whole of the licensed indication, as agreed in the scope, should be submitted by the applicant company. Where a medicine receives a licence extension, AWMSG will appraise the medicine for the whole of the indication(s) covered by that licence extension. Where the medicine under consideration is newly licensed or has received a licence extension, the applicant company may highlight a specific population within the submission for which the medicine may be particularly advantageous, ensuring that evidence to support the subpopulation is included. In such cases AWMSG may consider a restricted recommendation, whereby the medicine would not be recommended for use outside of this restriction.

What medicines are eligible for appraisal under AWMSG's policy for appraising a medicine to treat a very rare disease?
This policy applies in exceptional circumstances only:

- to medicines for conditions that have small patient populations who have limited or no treatment options; and
- where the uniqueness of the disease poses significant challenges in terms of evidence generation.

AWMSG will consider medicines as eligible for appraisal under its very rare disease policy if the medicine meets all four of the eligibility criteria outlined in the policy document available on the AWTTC website at awttc.nhs.wales.

How are medicines to treat very rare diseases considered?
AWMSG recognises that evidence generation can be challenging in certain populations, such as medicines for treating rare diseases. In these specific circumstances, AWMSG and NMG might be able to accept a higher degree of uncertainty when making recommendations. AWMSG and NMG will consider how the nature of the condition or medicine affects the ability to generate high-quality evidence, before applying greater flexibility.

How are medicines to treat severe diseases considered?
A review of AWMSG's health technology assessment (HTA) methods and processes led to the implementation of a policy for appraising medicines to treat severe conditions (available on the AWTTC website at awttc.nhs.wales). The new severity modifier will benefit a broader range of conditions (both end-of-life and non-end-of-life indications) and people living with seriously debilitating conditions. Application of the severity modifier will more accurately reflect social values and preferences. AWMSG will apply the same severity weightings as NICE to ensure HTA methods are aligned, thereby facilitating more equitable access to medicines in Wales.

When appraising a medicine, how will AWMSG consider the severity of the condition being treated?
AWMSG recognises society's priority for the expensive relief of a very serious condition over the relatively inexpensive relief of a mild discomfort when appraising a medicine for a severe condition. Severity is defined as the future health losses of people living with the condition who are receiving standard NHS care (that is, other current treatments or best supportive care). To assess the severity of a condition,

AWMSG will consider both absolute and proportional quality-adjusted life-year (QALY) shortfalls.

The absolute or proportional QALY shortfall value will determine what weighting is applied to the QALYs for a medicine. AWMSG may assign a greater weighting to QALYs if the assessments of QALY shortfall show that the medicine is to treat a condition that has a high degree of severity. Further information on how the severity of a condition is assessed can be found in the policy document for appraising medicines for severe conditions, available on the AWTTC website at awttc.nhs.wales.

Does AWMSG appraise biosimilar medicines?
AWMSG does not normally appraise biosimilar medicines. Existing Health Technology Appraisal (HTA) advice for the 'reference' medicine, published by AWMSG or NICE, will automatically apply for biosimilar medicines licensed for the same indication and in the same population as the 'reference' medicine. In the absence of advice for the 'reference' product, the biosimilar medicine is not endorsed for use within NHS Wales.

Does AWMSG consider equity when appraising a medicine?
Yes. AWMSG considers equity of patients within NHS Wales. When presenting an overview of the submission at the AWMSG public meeting, the All Wales Therapeutics and Toxicology Centre (AWTTC) Appraisal Lead highlights whether the medicine is available in the rest of the UK, either via a commissioning route or via health technology appraisal. This clarification was introduced in 2014. This information is also included in the AWTTC assessment of licence extensions for paediatric use.

In addition, in circumstances where the National Institute for Health and Care Excellence (NICE) does not recommend a medicine on grounds of lack of cost-effectiveness, but the medicine is available in England via a commissioning route, then the holder of the marketing authorisation may re-engage with AWMSG. The application must include a Wales Patient Access Scheme (WPAS) but may also include additional information not included in the submission to NICE.

How does AWMSG prioritise appraisals?
Appraisals are scheduled according to the submission dates. Prioritising criteria may be applied if the number of appraisal submissions received exceeds the AWMSG meeting capacity. Prioritisation when required will include input from Welsh Clinical Networks, commissioners and others within NHS Wales based on clinical need.

When is the appraisal date confirmed?
Following submission of Form B/C by the applicant company, the All Wales Therapeutics and Toxicology Centre (AWTTC) will confirm by email the appraisal scope and schedule. In the case of a licence extension to a medicine for paediatric use, confirmation is after receipt of Form A.

If AWMSG decides an appraisal is required, what is the timescale?
A completed Form B or C can be submitted to the All Wales Therapeutics and Toxicology Centre (AWTTC) before the medicine receives marketing authorisation, and up to three months after. This is also the case for submissions for licence extensions for paediatric use.

However, it is only on receipt of marketing authorisation that AWTTC will schedule the appraisal and confirm dates of meetings. Potential dates of the New Medicines Group (NMG) and AWMSG meetings will be offered and confirmed with the applicant company. The appraisal process flowcharts on the AWMSG website outline appraisal timelines. The maximum timescale for a limited submission process will be the same as for a full submission, i.e. six months. AWTTC will consult the applicant company should an opportunity arise for a limited submission to be scheduled for appraisal earlier than this; the appraisal may proceed with the earlier timelines following agreement from the applicant company. In the case of a submission that is eligible for the licence extension for paediatric use process, the maximum timescale should be three months.

When is the scope of the appraisal clearly defined?
The All Wales Therapeutics and Toxicology Centre (AWTTC) suggests the appraisal scope in writing (email or letter) when they inform the applicant company whether a full submission (Form B) or a limited submission (Form C) is required. The appraisal scope and the dates of the New Medicines Group (NMG) and AWMSG meetings are subsequently confirmed by AWTTC on receipt of Form B/C, following an initial review of the submission for completeness and appropriateness. All attempts to clarify any outstanding issues in relation to the scope should be made by either AWTTC or the applicant company prior to the production of the AWMSG Secretariat Assessment Report (ASAR) and the appraisal by the NMG. If NMG considers a redefinition of the scope essential, the appraisal may be adjourned pending clarification.

In the case of licence extensions to medicines for paediatric use, AWTTC confirms the appraisal scope and timelines following a review of the submission (Form A) for completeness and appropriateness, and clarification of any outstanding issues.

Who do I contact for clarification of the appraisal process or to address any outstanding issues?
Clarification of any aspect of the appraisal process may be sought from the All Wales Therapeutics and Toxicology Centre (AWTTC) at: awttc@wales.nhs.uk or on: 029 218 26900.

Appraisal submission forms

What is the role of Form A?
Form A provides the information required for the All Wales Therapeutics and Toxicology Centre (AWTTC) to decide whether a medicine requires appraisal by AWMSG. Form A should be completed for all newly licensed products, each new indication and/or formulation. Form A must be completed regardless of whether the product fits one or more of the exclusion criteria even if a submission has been forwarded to the National Institute for Health and Care Excellence (NICE) or the Scottish Medicines Consortium (SMC). **Early submission of Form A is encouraged**. It is essential that applicant companies refer to the 'AWMSG guidance notes' for submitting Forms A, B and C available on the AWTTC website at awttc.nhs.wales when compiling their submission. Failure to do so may result in an inadequate submission.

When should Form A be submitted?
Form A should be submitted as early as possible and before marketing authorisation is received. In the case of licence extensions for paediatric use, when certain criteria are met, this is the only form that is required to be completed by the applicant company.

When should the AWMSG Very Rare Diseases (VRD) Form be submitted?
When completing Form A, an applicant company will be asked to indicate if, in its view, their medicine has been developed to treat a very rare disease. When an applicant company judges its medicine will be used to treat a very rare disease, the AWMSG appraisal process requires the company to complete the Very Rare Diseases (VRD) Form (available on the AWTTC website at awttc.nhs.wales). The completed VDR Form should be sent to AWTTC at the same time as the Form A, to avoid delays in the appraisal process. AWTTC will then inform the applicant company whether their medicine is eligible to be appraised under the AWMSG Very Rare Disease policy. This decision is required before the applicant company submits Form B.

Does the Summary of Product Characteristics (SPC) need to be submitted with Form A?
Where available, an SPC should be included with the submission (a draft SPC is accepted). However, absence of an SPC does not preclude a company from submitting Form A to the All Wales Therapeutics and Toxicology Centre (AWTTC).

What is the timescale for submitting Form B or C?
A completed Form B or C can be submitted to the All Wales Therapeutics and Toxicology Centre (AWTTC) before the medicine receives marketing authorisation and up to three months after. An appraisal date will not be scheduled until marketing authorisation is received and the applicant company has provided a complete submission, i.e. for a full submission (Form A and Form B), or a limited submission (Form A and Form C).

Does the All Wales Therapeutics and Toxicology Centre (AWTTC) accept unlicensed comparators?
The applicant company should provide information on comparator treatment(s) based on current standard care in NHS Wales, i.e. what is considered to be “routine practice” and may potentially be displaced. Comparators licensed for the indication under consideration should usually be included; however, AWMSG will also consider unlicensed comparators where it is deemed appropriate to do so. For some medicines, it may be appropriate to consider more than one comparator (e.g. if practice is varied, or if current therapy is unlicensed).

What if the comparator medicine has an associated simple Patient Access Scheme?
In order to maintain confidentiality AWMSG will not share the details of a simple Patient Access Scheme for a comparator medicine with the company making an application to AWMSG for appraisal of a new medicine. To enable AWMSG to explore the impact of using the actual cost of the comparator in the analysis, the company applying for appraisal of a new medicine should model the cost-effectiveness of their medicine using a range of potential discounts for the comparator.

Does the All Wales Therapeutics and Toxicology Centre (AWTTC) accept data relating to a licensed comparator outside its licensed dose?
AWMSG normally requires comparator data relating to the dose which has been licensed as stated within the Summary of Product Characteristics (SPC). Exceptional circumstances should be discussed in advance of proceeding with the submission.

Can the applicant company submit commercial/academic in confidence data?
Applicant companies should attempt to minimise the amount of data marked as 'commercial/academic in confidence' provided as part of the Form A, B or Form C submission, in order to ensure the transparency of the decision-making process. If some data are deemed confidential (according to the guidelines agreed by the Association of British Pharmaceutical Industry [ABPI]) it should be clearly marked as such. Information marked 'Confidential' will be made available to members for discussion, but will not be included in the meeting papers uploaded to the AWMSG website. It should be noted that due to the 'public nature' of AWMSG appraisals, 'commercial/academic in confidence' information may be referred to verbally during the formal appraisal. However, where a company is required to respond to extensive questions from AWMSG members about commercial in confidence information during an appraisal held in public, the company may request of the Chair that this will take place within a closed session of the meeting where the public will not be present. Submissions which include a confidential patient access scheme will be appraised by AWMSG in private.

What documents will be uploaded to the AWMSG website prior to the AWMSG meeting?
For full/limited submissions, the documents placed on the website prior to the AWMSG meeting are the Preliminary Appraisal Recommendation (PAR), the company response to the PAR (CR/PAR) and a non-confidential version of the AWMSG Secretariat Assessment Report (ASAR). Any 'commercial/academic in confidence' data would be embargoed from the website version until 12 months after completion of the research (patient access schemes will remain confidential. The draft recommendation will be uploaded to the AWMSG website prior to the AWMSG meeting for submissions that meet the criteria to be appraised via the process for licence extensions for paediatric use.

Are the completed submissions (Form A, Form B or Form C) posted on the AWMSG website?
No, only basic information from Form A such as generic name, trade name and therapeutic indication is placed on the AWMSG website as part of the Appraisal Work Programme under the 'Appraisals in progress' section, indicating that the medicine has been submitted for consideration. This table also states whether the medicine met the criteria for appraisal by AWMSG. Form B/C is not posted on the AWMSG website.

What is the role of Form B/C?
Form B/C provides comprehensive information and is used by the All Wales Therapeutics and Toxicology Centre (AWTTC), together with additional relevant information, in the preparation of their assessment report (the AWMSG Secretariat Assessment Report [ASAR]). Form B/C is part of the meeting documentation provided to members of the New Medicines Group (NMG) who make the Preliminary Appraisal Recommendation (PAR) to AWMSG.

How does a company know if a medicine meets AWMSG's criteria for appraisal as a licence extension for paediatric use?
Form A provides the information needed to determine if a medicine meets AWMSG's criteria for appraisal as a licence extension for paediatric use. Where these criteria (see below) are met, the information in Form A is used by the All Wales Therapeutics and Toxicology Centre (AWTTC) to prepare a brief assessment report for AWMSG. The applicant company are notified by AWTTC in writing within 4 weeks from receipt of Form A if the medicine meets the criteria for this process.

The final decision as to what type of submission is required is that of AWMSG. The medicine must meet all of the following criteria to be appraised by AWMSG under the process for paediatric licence extensions:

- **The licence extension must be for use of the medicine in patients aged under 18 years**
- **The medicine has been accepted for use in adults (aged 18 years and older) by AWMSG or the National Institute for Health and Care Excellence (NICE); and that advice or guidance must still apply**
- **The licence extension must match the adult indication that was accepted for use by AWMSG or NICE, except for the target age group of patients**

AWMSG reserves the right to request a full submission in relation to any medicine at any time during the process. The decision of AWMSG in this respect is final and binding.

How does a company know if a medicine requires a full (Form B) or limited (Form C) submission?
The nominated contact for the applicant company will be notified by the All Wales Therapeutics and Toxicology Centre (AWTTC) in writing whether the submission meets the criteria for AWMSG appraisal and, if so, whether a Form B or Form C is required. AWTTC aim to provide feedback within two weeks and will inform the applicant company if there is a delay. A flow diagram setting out the decision process for a full or limited submission is available on the AWMSG website.

The final decision as to whether a full submission (Form B) or limited submission (Form C) is required is that of AWMSG. A limited submission (Form C) may be deemed appropriate by AWMSG in any of the following circumstances (where a medicine is not a new chemical entity or for a new licensed therapeutic indication [New Target Disease]):

- **A significant new formulation which has a pro-rata or lower cost per treatment**
  e.g. slow release, new chemical salt of established medicine

- **A licence extension which is deemed minor by AWMSG**

- **If the anticipated usage in NHS Wales is considered by AWMSG to be of minimal budgetary impact**

- **If the estimated difference in cost compared with the appropriate comparator(s) is deemed by AWMSG to be small**

- **Follow on biologic medicines, i.e. a biologic product which is identical to an existing product (produced on the same production line in the same factory) but with a different product licence**

When a limited submission (Form C) is deemed appropriate by AWMSG, applicant companies may provide less information than routinely required in completion of Form B and aim to prove clinical effectiveness/equivalence. However, evidence of budgetary impact in comparison to the comparator medicine(s) should be demonstrated. Applicant companies should refer to the limited submission process (Form C) and the 'AWMSG guidance notes on Form C' for further information. Applicant companies will be informed in writing (email or letter) whether a full submission (Form B) or a limited submission (Form C) is required, after consideration of Form A. AWMSG reserves the right to request a full submission in relation to any medicine at any time during the process. The decision of AWMSG in this respect is final and binding.

Is guidance available on how to complete Form A, Form B and Form C?
Essential information on how to complete all of the submission forms is available under 'AWMSG guidance notes' on the AWMSG website. It is vital that applicant companies refer to this guidance, as failure to do so may result in an inadequate submission. Further advice is available from the All Wales Therapeutics and Toxicology Centre (AWTTC) if required at: awttc@wales.nhs.uk or on: 029 218 26900.

Where can I find Welsh unit cost data?
NHS bodies in Wales produce various annual costing returns which are submitted to the Financial Information Strategy Development Programme (FISDP) for collating on behalf of Welsh Government. The Welsh Costing Return 2 (WCR 2) is one such submission, and provides information on the costs of inpatient and day-case Healthcare Resource Groups (HRGs) at a finished consultant episode (FCE) level and by speciality (e.g. general surgery, cardiology).

WCR 2 returns are submitted to FISDP at an elective and emergency level for inpatient activity and consolidated to produce an All Wales average HRG cost per FCE (but not at speciality level).

Access to the All Wales average HRG costs per FCE is available to all of the NHS bodies in Wales via the Welsh NHS intranet; or alternatively by contacting the FISDP.

The latest information available is the 2007/08 All Wales average HRG costs, which have been produced using version 3.5 HRGs. This means that unlike their English counterparts, they still carry the three-character HRG code (e.g. E28 for cardiac arrest, as opposed to EB05Z, for version 4.0 HRGs).

For information, Wales does not trim its bed days, as in England, and critical care costs are produced as part of the Welsh Costing Return 1 (WCR 1) specialty analysis return. Welsh critical care costs are not included in the HRG costs.

Can additional information be provided to the All Wales Therapeutics and Toxicology Centre (AWTTC) after submission of Form B/C?
The inclusion of new evidence into the appraisal process after receipt of form B or C is extremely rare and its inclusion is at the discretion of AWTTC, which will be on a case by case basis. AWMSG reserves the right to suspend the appraisal process at any stage in order to seek clarification of an outstanding issue. Form B asks for 'details of ongoing studies from which additional evidence is likely to be available in the next 6–12 months. If additional information (previously highlighted in that section) becomes available, the applicant company should contact AWTTC who will inform as to whether it can be included in the AWMSG Secretariat Assessment Report (ASAR). This is dependent on timelines. No other information will be accepted. If 'new evidence' is not accepted, a subsequent resubmission will be timetabled pragmatically into the work programme. A resubmission would be timetabled at the earliest convenience; however, there is no guarantee of a definite slot and this could take up to 12 months.

Can additional information be provided to the All Wales Therapeutics and Toxicology Centre (AWTTC) after submission of Form A for a medicine that meets the appraisal process criteria for licence extensions for paediatric use?
The applicant company may be asked to submit further information for clarification or to address any outstanding issues. AWMSG reserves the right to suspend the appraisal process at any stage in order to seek clarification of an outstanding issue. The inclusion of new evidence into the appraisal process that has not been requested by AWTTC after receipt of Form A for a licence extension for paediatric use is extremely rare. Its inclusion is at the discretion of AWTTC, and will be on a case by case basis.

Would a request for a limited submission (Form C) preclude the need for a full submission (Form B)?
AWMSG reserves the right to request a full submission (Form B) in relation to any medicine at any time during the process. The decision of AWMSG in this respect is final and binding.

What if the Form A meets the criteria for a limited submission or to be appraised as a licence extension for paediatric use, and the manufacturer has indicated in Form A that they wish to submit a Wales Patient Access Scheme (WPAS)?
This would be assessed on a case by case basis. A limited submission or a licence extension for paediatric use submission would usually be accepted for a simple WPAS; however, a complex scheme would usually require a full submission in both cases.

Is the process for considering limited submissions (Form Cs) different to that for full submissions (Form Bs)?
The New Medicines Group (NMG) considers full and limited submissions and agrees a Preliminary Appraisal Recommendation (PAR). AWMSG subsequently considers full and limited submissions and agrees a Final Appraisal Recommendation (FAR). As the level of detailed information required within a limited submission is less than that of a full submission, the level of discussion will usually be less. Following endorsement by Welsh Government of the AWMSG recommendation for a limited or full submission, the advice will be posted on the AWMSG website and disseminated electronically to NHS Wales.

Is the process for considering licence extensions for paediatric use different to that for full or limited submissions (Form B/Cs)?
AWMSG make a recommendation based on an assessment conducted by the All Wales Therapeutics and Toxicology Centre (AWTTC) to confirm clinical effectiveness and budgetary impact. This assessment is mainly based on the information obtained from the initial submission (Form A. The draft recommendation is shared with the applicant company and posted on the AWMSG website prior to the AWMSG meeting. Clinical expert and patient/carer/patient organisation opinion will not routinely be requested, and the submitting company do not need to attend the AWMSG meeting, although they are welcome to do so.

Since such submissions do not require the medicine to be considered by the New Medicines Group (NMG), it is anticipated that the recommendation outcome is likely to be obtained in a shorter timeframe to that of full or limited submissions. Following endorsement by Welsh Government of the AWMSG recommendation, the advice will be posted on the AWMSG website, the same as for a limited or full submission, and disseminated electronically to NHS Wales. Where there is an existing AWMSG recommendation in adults, this will be merged with the new recommendation for use of the medicine in paediatric patients.

What are the consequences if a submission (Form A, Form B or Form C) is requested by the All Wales Therapeutics and Toxicology Centre (AWTTC) but not received within the appropriate timelines?
Form A should be submitted as soon as possible and before marketing authorisation is received) regardless of whether a submission has been forwarded to the National Institute for Health and Care Excellence (NICE) or the Scottish Medicines Consortium (SMC).

The complete submission (i.e. full submission [Form A and B], limited submission [Form A and C], or in the case of licence extension for paediatric use submissions, Form A only) should be submitted to AWTTC as soon as possible and before marketing authorisation is granted and, at the very latest, within three months of receipt of marketing authorisation. In the event that a company submission is requested and is not forthcoming, the following two options are available to AWMSG:

a) In the absence of a submission from the company, AWMSG will issue a statement of advice (posted on the AWMSG website) confirming **the medicine cannot be endorsed for use within NHS Wales** – *a decision made by AWMSG.* This statement will be ratified by Welsh Government.

b) AWMSG will appraise the medicine using publicly available information – *if directed to do so by AWMSG.*

AWMSG considers specialist network opinion, demand from within NHS Wales and policy imperatives when making its decision on how best to proceed with regard to non-submissions.

Applicant companies who are planning to submit Form A, B, or C should be aware that appraisal dates cannot be confirmed until the complete submission is received by AWTTC and the appraisal scope has been agreed. A delay in submitting will result in a delay in the appraisal process.

Funding for use of a medicine that falls within the AWMSG appraisal criteria within NHS Wales is very unlikely prior to an AWMSG appraisal.

Applicant company input into appraisal process

Does the applicant company have an opportunity to preview the AWMSG Secretariat Assessment Report (ASAR) before it is provided to the New Medicines Group (NMG) members?
Yes. The applicant company has a period of ten working days to provide a short summary response to the draft ASAR, i.e. the company response to the ASAR (CR/ASAR). This is the only opportunity for the applicant company to highlight in writing any differences in scientific interpretation and identify factual inaccuracies or typographical errors. No additional clinical or health economic evidence should be submitted (unless previously stated in the Form B/C submission and agreed with the All Wales Therapeutics and Toxicology Centre (AWTTC). The applicant company is also requested to confirm the information which is of a 'commercial/academic in confidence' nature. The CR/ASAR will form part of the NMG appraisal documentation along with the ASAR itself, the Form B/C and written evidence from clinical experts and patient organisation(s) (where available). Failure to provide a response to the draft ASAR by the applicant company will not delay the process.

Does the applicant company have an opportunity to preview the Preliminary Appraisal Recommendation (PAR) before it is provided to AWMSG members?
Yes. Within five working days of the New Medicines Group (NMG) meeting, the PAR will be forwarded to the applicant company **for comment**. The company response to the PAR (CR/PAR) will be included with the AWMSG meeting documentation and will be placed on the AWMSG website approximately ten working days before the AWMSG meeting.

What is the role of the applicant company in relation to the process for appraising medicines developed to treat very rare diseases?
If the applicant company judges that its medicine meets the AWMSG criteria to be appraised under the medicines to treat very rare diseases policy (available at awttc.nhs.wales), then the company should complete the very rare diseases (VRD) form. See the section above 'Appraisal Submission Forms' for further information. Confirmation from AWTTC that the medicine is eligible to be appraised under the very rare disease policy should be received before submitting Form B.

After receiving the Form B submission, the AWMSG appraisal process for medicines to treat very rare diseases is similar to the process for all other medicines. However, if a medicine to treat a very rare disease receives a negative recommendation by the New Medicines Group (NMG), the applicant company can request that a meeting of the Clinician and Patient Involvement Group (CAPIG) be convened. The applicant company will be invited to provide a statement, attend and participate in discussions, and will leave the meeting before the CAPIG template is finalised.

Can the applicant company challenge the decision of the Very Rare Diseases Panel?

The medicines to treat a very rare disease policy explains that an applicant company can challenge the panel's decision, if it thinks that the eligibility criteria have not been applied appropriately. The applicant company should provide adequate explanation of the reasons for their challenge and submit them via email to awttc@wales.nhs.uk within 7 calendar days of notification of the panel's decision.

What is the role of the applicant company in relation to the process for appraising medicines developed to treat rare diseases?

The applicant company will be asked when completing Form A to indicate if, in its view, the medicine will be used to treat a rare disease (that is, a medicine with orphan status). When completing Form B, the company has the opportunity to give additional information about factors that are particularly important to AWMSG's considerations for medicines developed to treat rare diseases.

What is the role of the applicant company in relation to the process for appraising a medicine developed to treat a severe condition?

The appraisal process for a medicine to treat a severe condition aligns with AWMSG's process for appraising other medicines (see AWMSG Guidance on appraisal structure and evidence). The applicant company will be asked in Form A to indicate if, in their view, their medicine has been developed to treat a severe condition. An opportunity to give further evidence and explanation is provided in Form B.

When submitting to AWMSG, the applicant company should make it clear in the Form B whether it considers the severity modifier to be applicable. AWTTC will take this into account when assessing the information and preparing the AWMSG Secretariat Assessment Report (ASAR). In the ASAR, AWTTC will state its view about whether the severity modifier should apply. If the severity modifier is considered not to apply, the applicant company will have the opportunity to challenge this decision in its response to the ASAR. Information regarding the severity modifier can be found in the policy for appraising a medicine to treat a severe condition (available on the AWTTC website at **awttc.nhs.wales**).

Does the applicant company have an opportunity to preview the final AWMSG Secretariat Assessment Report (ASAR) before it is provided to AWMSG members?

Yes. The final ASAR will be forwarded to the applicant company after the New Medicines Group (NMG) meeting **for information only**. Opportunity to comment on the draft ASAR is afforded to the applicant company before the NMG meeting. In the event that the applicant company provides additional information or comments relating to the final ASAR in their response to the Preliminary Appraisal Recommendation (PAR), the All Wales Therapeutics and Toxicology Centre (AWTTC) reserves the right to withhold the response as the additional information/comment(s) would not have been considered by NMG. Failure to provide a response to the PAR by the applicant company will not delay the process.

The patient/carer view

How can patients/carers/patient organisations directly input into the AWMSG appraisal process?
The AWMSG appraisal process offers patients/carers/patient organisations an opportunity to ensure their views are heard and provides them with a means to really make a difference. Patients/carers/patient organisations can have a voice in an appraisal process which could ultimately have a significant impact on patients and/or carers living in Wales.

An invitation is extended to patients/carers/patient organisations to complete a questionnaire to outline their experience of the disease/condition in question and the associated treatments, and to explain why the needs of the patient/carer are currently met or not met. The All Wales Therapeutics and Toxicology Centre (AWTTC) welcome any information that might help us understand how these health problems affect patients and/or carers. Patients/carers/patient organisations are often able to provide additional insight which is invaluable in considering whether a medicine should be available to patients within NHS Wales.

Patients/carers/patient organisations can help inform AWMSG of the real effects on patients and bring a human dimension to the assessment, and this input will have an impact on decisions on which medicines should be funded ahead of a technology appraisal by the National Institute for Health and Care Excellence (NICE).

A questionnaire can be downloaded from the AWMSG website and we ask that views be submitted to AWTTC by post or email (awttc@wales.nhs.uk) six weeks prior to the New Medicines Group (NMG) meeting in time for all the appraisal information to be collated. The AWMSG meeting is open to the public and patients/carers/patient organisations would be welcome to join the audience.

AWTTC do not directly seek views as part of the licence extensions for paediatric use process. AWTTC however welcomes individual patient views and encourage patients/carers/patient organisations to actively refer to the new medicines needing your views page on the AWMSG website and to complete a questionnaire.

Are all appraisals by AWMSG held in public?
There may be occasions where the appraisal of a medicine by AWMSG is held in private. This is usually because the submission made by the applicant company contains commercially sensitive and confidential information i.e. the submission contains a confidential patient access scheme. Members of the public will not be able to observe that part of the meeting and this will be made clear on the agenda. However, when the meeting recommences in public, the recommendation of AWMSG will be announced. Please contact the All Wales Therapeutics and Toxicology Centre (AWTTC) for further information and/or check the relevant meeting agenda on the AWMSG website for details.

Will the completed patient/carer questionnaires be posted on the website?
No. The patient/carer questionnaires will not be placed in the public domain. They will, however, be circulated to the New Medicines Group (NMG) and AWMSG members as part of the appraisal meeting documentation. The issues highlighted in the questionnaires may be discussed at the AWMSG meeting in public; however, the patient organisation questionnaires will only be viewed by members. Individual

patients/carers submissions will be made anonymous. Patient organisations may also remain anonymous by ticking the relevant box on the questionnaire.

How are patient organisations identified and invited to make a submission?
The All Wales Therapeutics and Toxicology Centre (AWTTC) welcomes individual patient views and encourages patients/carers/patient organisations to actively refer to the new medicines needing your views section on the AWMSG website and to complete a questionnaire. For full and limited submissions, AWTTC also uses a standard internet search to identify patient organisations. In addition, the pharmaceutical company suggests organisations to contact. AWTTC then invite the relevant patient organisations to fill in a questionnaire.

Why should you, as a patient/carer/patient organisation, provide your views?
You can outline your experience of the disease/condition in question and any experience you might have of the associated treatments, explaining why your needs are currently met or not met. We welcome any information that might help us understand how these health problems affect patients and/or carers. Patients/carers/patient organisations are often able to provide additional insight which is invaluable in considering whether a medicine should be available to patients within NHS Wales. You can help inform us of the real effects on patients and bring a human dimension to the appraisal, and this input will have an impact on which medicines should be funded.

What should I do if I have any queries or want to learn more about the AWMSG appraisal process?
You should telephone (029 218 26900) or email (awttc@wales.nhs.uk) the All Wales Therapeutics and Toxicology Centre (AWTTC) and direct your enquiry to Mrs Ruth Lang, Head of Liaison & Administration.

Is there a forum for liaison between AWMSG and patient support groups?
The Patient and Public Interest Group (PAPIG) held its first meeting on Wednesday 9 October 2013 in the Routledge Academic Centre at University Hospital Llandough. Meetings included discussion about the appraisal processes, medicines development through to clinical trials and patients' medicine taking behaviour. Lay representatives from AWMSG and the sub-groups have attended and explained their role. PAPIG has considered barriers to engagement with AWMSG and provided feedback on the Patient and Public Engagement (PPE) Strategy. Members have also given feedback on the AWMSG website, which has been redesigned and updated with a section specifically tailored to patients, carers, patient organisations and members of the public.

If you are interested in being involved, please contact Ruth Lang on telephone 029 218 26900 or email awttc@wales.nhs.uk.

Clinical experts

What is the role of the clinical expert?
Clinical experts are contacted by the All Wales Therapeutics and Toxicology Centre (AWTTC) for advice on current practice in NHS Wales and advice on appropriate comparators. Such experts help set the clinical scene and outline where, in their view, the new medicine sits within current therapy in NHS Wales. On receipt of Form

B/C, AWTTC invites clinical experts to submit their views in the form of a questionnaire. Questionnaires are not routinely requested as part of the licence extensions for paediatric use process.

How are clinical experts selected?
AWMSG seek up to six clinical expert nominations via the appropriate Welsh professional society or clinical network or Medicines and Therapeutics Committees (MTCs). In the absence of appropriate expertise in NHS Wales, AWMSG will seek clinical input from outside Wales.

In what form is the clinical expert opinion provided?
The nominated clinical experts are contacted and asked to complete a questionnaire. The completed questionnaires are considered at the New Medicines Group (NMG) meeting and are also provided to AWMSG members prior to the AWMSG meeting. The questionnaires will not be published on the AWMSG website. Questionnaires are not routinely requested as part of the licence extensions for paediatric use process. Clinical expert opinion, when sought as part of this process, will however be highlighted in the AWTTC assessment.

Are clinical experts asked to declare any interests?
Nominated clinical experts are asked to complete and return a declaration of interest form with their questionnaire.

Can clinicians do anything to encourage appraisal by AWMSG, particularly if the pharmaceutical industry has not engaged in the appraisal process?
Yes, you can encourage the relevant pharmaceutical company to engage in the appraisal process, and you can highlight to the All Wales Therapeutics and Toxicology Centre (AWTTC) the need for advice within NHS Wales. In the absence of engagement, AWMSG may instruct an appraisal using publicly available information. This is more likely to occur in when evidenced by clinical support.

The New Medicines Group (NMG) meeting

Is the applicant company involved in the New Medicines Group (NMG) meeting?
The NMG meeting is held in private and the applicant company is not invited to attend. However, the company may wish to nominate a ‘contact’ to be on stand-by and contactable by telephone in the unlikely event that an issue arises during the NMG appraisal. The applicant company’s written response to the AWMSG Secretariat Assessment report (ASAR) is included in NMG’s meeting documentation.

What is the role of the Lead Assessor at NMG?
The Lead Assessor will address the NMG meeting and present all the information pertaining to a particular appraisal.

Is the applicant company informed of the New Medicines Group (NMG) Preliminary Appraisal Recommendation (PAR)?
Yes. Within five working days from the NMG meeting, the PAR will be forwarded by email, offering the applicant company an opportunity to provide a formal company response to the PAR (CR/PAR). This response will be included with the AWMSG meeting documentation and will be placed on the AWMSG website. The AWMSG Secretariat Assessment Report (ASAR) will be forwarded separately to the applicant

company for information only – **no comments in relation to the ASAR will be accepted by the All Wales Therapeutics and Toxicology Centre (AWTTC) at this stage in the process**. Failure to provide a response to the PAR by the applicant company will not delay the process.

Can the New Medicines Group (NMG) request additional data or seek clarification on any issue and adjourn the preliminary appraisal?
Yes. NMG can request an adjournment whilst seeking clarification of any outstanding issues. The All Wales Therapeutics and Toxicology Centre (AWTTC) will inform the applicant company of the reason for the adjournment, address the outstanding issues and reschedule the appraisal by NMG.

The AWMSG public meeting

What information is considered by AWMSG when making their recommendation?
AWMSG members receive the following documentation and are asked to apply a broad strategic/societal overview when considering the Preliminary Appraisal Recommendation (PAR) made by the New Medicines Group (NMG).

1. The AWMSG Secretariat Assessment Report (ASAR)
2. The Preliminary Appraisal Recommendation (PAR)
3. The company response to the PAR (CR/PAR)
4. The patient organisation submission(s) (if provided)
5. The clinical expert(s) views (if provided)

In the case of licence extensions for paediatric use, AWMSG members receive the All Wales Therapeutics and Toxicology Centre (AWTTC) assessment and draft recommendation.

How often are AWMSG meetings held?
Up to ten AWMSG meetings are scheduled per year and dates of the forthcoming meetings are displayed on the AWMSG website. Papers are uploaded to the website approximately ten days prior to the meeting.

When are the Preliminary Appraisal Recommendation (PAR) and the company response to the PAR (CR/PAR) posted on the AWMSG website?
All AWMSG meeting documentation is posted on the website approximately ten working days prior to the publicly held meeting. Papers submitted after the ten day deadline will only be accepted after consideration by the AWMSG Chair.

Is the applicant company involved in the AWMSG meeting?
For Form B/C submissions, the All Wales Therapeutics and Toxicology Centre (AWTTC) strongly encourage applicant companies to attend the AWMSG public meeting, although there is no obligation for them to do so. Prior to the meeting, AWTTC invites the company to nominate two representatives - one to respond to issues relating to the case for cost-effectiveness and one to respond to issues relating to clinical effectiveness. The Chair may or may not invite applicant companies into the discussion. Applicant companies with a licence extension for paediatric use submission do not need to attend the AWMSG public meeting, but are welcome to do so. However, if the applicant company has opted to attend, the

company representative(s) may be asked to answer questions from members, should there be any.

The Chair will ask the submitting applicant company representative(s) in attendance to confirm whether or not they are satisfied that all relevant issues have been addressed prior to concluding the appraisal. If a representative is not **employed** by the applicant company, please inform AWTTC at least six weeks prior to the appraisal.

What are the implications of a positive/negative AWMSG recommendation?
AWMSG advice has no impact on the licensed status of the technology and the inherent implications associated with this. A negative recommendation would not impact on the clinical freedom of the prescriber. A positive recommendation by AWMSG, subsequently endorsed by Welsh Government, places an obligation on the Service in Wales to fund accordingly. AWMSG advice is interim to Technology Appraisal Guidance issued by the National Institute for Health and Care Excellence (NICE) should it be subsequently published.

What is the context of the AWMSG appraisal?
The Chair confirms that in making their recommendation to AWMSG, the New Medicines Group (NMG) has considered the clinical and cost-effectiveness issues in detail. He reminds members that there is no requirement for AWMSG to repeat the detailed discussions held at NMG. The Chair directs AWMSG members to seek clarification of any outstanding issues in relation to clinical or cost-effectiveness, the company response to the Preliminary Appraisal Recommendation (CR/PAR), the clinical expert questionnaire(s), the patient organisation submission(s), and take account of any societal or budget impact issues.

In the case of a licence extension for paediatric use, the medicine will not have been considered by NMG. The Chair confirms that a draft recommendation has been presented to AWMSG for consideration and approval, based on the All Wales Therapeutics and Toxicology Centre (AWTTC) assessment. The Chair asks AWMSG members to confirm if there are any outstanding issues or points for clarification.

How is the appraisal process conducted at the meeting?
For Form B and C submissions, the Chair will invite the All Wales Therapeutics and Toxicology Centre (AWTTC) Assessment Lead to present the AWMSG Secretariat Assessment Report (ASAR) and clinical expert view to AWMSG members. The New Medicines Group (NMG) Chair (or AWTTC Assessment Lead) subsequently presents the Preliminary Appraisal Recommendation (PAR). AWMSG members will be invited to raise any issues in relation to the ASAR, the PAR, the company response to the PAR (CR/PAR), the clinical expert questionnaire(s) and the patient organisation submission(s). Delegates from the applicant company will be asked by the Chair to confirm there are no outstanding issues prior to concluding the appraisal.

In the case of a licence extension for paediatric use, the assessment lead will respond to any queries by email ahead of the meeting and will give a brief verbal summary of these at the meeting, if relevant. The Chair will ask AWMSG members to confirm if there are any outstanding issues prior to concluding the appraisal. If no issues are raised ahead of the meeting, it is expected there will be minimal or no discussion on the day.

AWMSG members will retire to vote in private and the Chair will subsequently announce the recommendation in public.

Who is involved in the decision making process?
The voting members of AWMSG (refer to AWMSG website for full details of membership).

Are all appraisals by AWMSG held in public?
Normally, yes. However, where a submission includes a **confidential** patient access scheme, the appraisal will be conducted in private. AWMSG's recommendation would normally be subsequently announced when the meeting recommences in the public domain. It should be noted that due to the 'public nature' of the AWMSG appraisal, certain 'commercial/academic in confidence' data may be referred to verbally during the formal appraisal.

Communication post–AWMSG meeting

What happens after a decision has been reached by AWMSG?
The AWMSG Chair normally announces the AWMSG recommendation at the publicly held AWMSG meeting. Confirmation of the AWMSG recommendation (the Final Appraisal Recommendation [FAR]) is forwarded to the applicant company within five working days of the AWMSG meeting. When AWMSG virtual meetings are held, the outcome of the appraisal will be emailed to the applicant company on the day of the meeting. For transparency, a notice will also be uploaded to the AWMSG website. Companies have 10 working days from the meeting to accept the recommendation or lodge a request for an independent review, the grounds for which should be submitted in writing to the Chair via the All Wales Therapeutics and Toxicology Centre (AWTTC). The process will not be delayed if companies fail to respond within this deadline. At the end of the ten-day period, and unless a request is made for an independent review (IR), AWTTC will forward AWMSG's recommendation to Welsh Government officials for ratification. Welsh Government officials consider the AWMSG recommendation and advise whether funding should be made available for the use of the medicine within NHS Wales. AWTTC contact the applicant company when ratification of AWMSG's recommendation has been received.

What are the timelines for ratification by Welsh Government of an AWMSG Final Appraisal Recommendation (FAR)?
No fixed timescale can be given as this is dependent on competing Welsh Government priorities. It is hoped that ratification will be received within two weeks from receipt of the AWMSG recommendation.

How is the applicant company notified of ratification by Welsh Government of an AWMSG Final Appraisal Recommendation (FAR)?
Upon receipt of ratification by Welsh Government, the All Wales Therapeutics and Toxicology Centre (AWTTC) will inform (by email) the nominated contact(s) from the applicant company.

How is NHS Wales notified of the AWMSG Final Appraisal Recommendation (FAR) and ratification by Welsh Government?
The FAR is posted on the AWMSG website and confirmation of ratification by Welsh Government to the AWMSG recommendation is disseminated by email to NHS Wales. Reference to appraisal advice issued may also be included in the Chief Medical Officer's update publication.

What role does the applicant company have in communicating the AWMSG recommendation?
In order to avoid confusion, communication of the AWMSG recommendation(s) should not take place until the recommendation(s) has/have been ratified by Welsh Government. Communications should quote the recommendation in full, including any restrictions.

What happens if final Technology Appraisal Guidance from the National Institute for Health and Care Excellence (NICE) becomes available for a medicine that has been appraised by AWMSG?
If Technology Appraisal Guidance is issued by NICE for the same medicine and indication as that appraised by AWMSG, a statement that AWMSG advice has been superseded by NICE guidance will be placed on the Final Appraisal Recommendation (FAR), with reference to the relevant NICE guidance.

Implementation

Is the AWMSG recommendation to the Service binding?
If a medicine is recommended by AWMSG, there is a requirement on health boards to provide funding to enable implementation as soon as is reasonably practicable and certainly within two months of ratification by Welsh Government.

"**RECOMMENDED FOR USE** within NHS Wales" applies to a medicine first in its class for that specific licensed indication. This places an obligation on health boards to make the medicine available and fund accordingly. Where a formulary exists, the medicine should be included.

"RECOMMENDED AS AN OPTION FOR USE within NHS Wales" applies to a medicine when it is not the only treatment available for a specific licensed indication. This places an obligation on health boards to make the medicine available for a patient who meets the clinical criteria set out in the guidance, subject to the clinical judgement of the treating clinician. Where a formulary exists, the medicine should be included and prescribing priority should be in accordance with local formulary decision. For the avoidance of doubt or confusion, when AWMSG recommends a medicine as **'an option',** this is an option for the clinician and patient to consider alongside other potential treatments, not an option for commissioners or providers to not make the treatment available.

Will extra funding be available to support the introduction of new medicines?
Yes. The Welsh Government's New Treatment Fund (NTF) was announced in January 2017. The fund will support health boards to introduce new, recommended medicines faster and more consistently across Wales. The fund is ring-fenced to ensure it is used for the intended purpose of supporting health boards to make all new medicines recommended by the National Institute for Health and Care Excellence (NICE) and AWMSG available faster and more consistently across

Wales. The fund will help ease the financial pressures that can be associated with the introduction of new medicines, providing health boards with the time to plan to invest in future years. New medicines recommended for an interim period by NICE will also be available in Wales within the same two month NTF implementation timeframe, provided the manufacturer offers NHS Wales the same or similar package, including price, as NHS England. The implementation timeframe will start once the package has been agreed.

How will AWMSG recommendations be implemented?
The All Wales Therapeutics and Toxicology Centre (AWTTC) will disseminate the recommendation (ratified by Welsh Government) electronically across NHS Wales. The information will also be posted on the AWMSG website at www.awmsg.org and details may be published in the Chief Medical Officer's update publication. The responsibility for the implementation of Welsh Government's decision lies with the commissioning bodies.

Will the industry have a role in implementing AWMSG recommendations?
The industry may wish to play a supportive role with implementation. Please also see the AWMSG Terms of Use.

How will the implementation of AWMSG recommendations, once ratified by Welsh Government, be monitored across NHS Wales?
Implementation of the National Institute for Health and Care Excellence (NICE) and AWMSG recommendations is included as a standard (Standard 12) in the document, "Healthcare Standards for Wales" that was published in May 2005. The monitoring of the implementation of all Healthcare Standards falls to Healthcare Inspectorate Wales (HIW). A Welsh Health Circular (2017) 001 has been issued by Welsh Government which clearly outlines the responsibility to make funding available as soon as is reasonably practicable and certainly within two months of the published recommendation. Auditing the uptake of AWMSG and NICE recommendations has also been included in the work programme of the Welsh Analytical Prescribing Support Unit (WAPSU).

Independent review (IR)

Is there a route for an applicant company to follow if they are unhappy with the outcome of an appraisal?
The AWMSG independent review (IR) process addresses both scientific disputes and concerns relating to process.

How soon after receiving confirmation of the AWMSG Final Appraisal Recommendation (FAR) will the applicant company need to request an independent review (IR)?
A request for an IR, with an outline justification, must be lodged in writing with the AWMSG Chair within ten working days of the AWMSG meeting at which the medicine was appraised (i.e. within two weeks from the meeting and announcement of the recommendation).

What does the applicant company need to do to trigger the independent review (IR) process?
The process of IR may be triggered (by the applicant company) using the procedures set out in the IR process available on the AWMSG website.

What is the procedure to address concerns relating to 'process'?
Significant steps have been introduced to allow dialogue between the All Wales Therapeutics and Toxicology Centre (AWTTC) and the applicant company during the appraisal process. Nevertheless, the applicant company may occasionally feel that insufficient time or opportunity was given for discussion of relevant issues and so may wish to lodge a complaint based on process. In such circumstances, a request for review of the process should be submitted to AWTTC who will forward this to AWMSG. Failing resolution, the complaint may be referred to the Welsh Government.

What is the procedure to address complaints relating to scientific disputes?
When the concerns of the applicant company relate to differences in scientific opinion and/or interpretation of data, an independent review (IR) may be the most appropriate mechanism to address the complaint.

Can the applicant company have access to the transcript of the AWMSG meeting at which the original decision was made?
Transcripts of AWMSG meetings are not routinely produced, but can be provided on application subject to payment of transcription costs. If an independent review (IR) proceeds and a meeting recording is provided to the IR Panel, then the applicant company may request a copy of the meeting recording at no additional cost.

Who sits on the independent review (IR) panel?
The IR panel will be appointed by the All Wales Therapeutics and Toxicology Centre (AWTTC) on advice from AWMSG and will comprise of seven members:

- Three members appointed from AWMSG itself (ideally but not exclusively members who, by reason of absence, have not been involved in the particular appraisal). One of these individuals will be appointed to chair the panel.

- Four members appointed from the Medicines and Therapeutics Committees (MTCs) in Wales and/or other respected experts in the relevant scientific field who may or may not work in Wales.

What are the responsibilities of the applicant company?
Applicant companies, in submitting an original application to AWMSG, have a duty and a responsibility to submit all relevant data in that application, as they do to the licensing authority.

Will the applicant company attend the independent review (IR) hearing?
Yes. The applicant company will be invited to attend the IR hearing.

What happens at the independent review (IR) hearing?
The IR Chair will decide upon the order of the day. The role of the IR panel is to investigate the complaint and make a recommendation to AWMSG as to whether they should reconsider the evidence. Should scientific support and advice be required, it will be provided by All Wales Therapeutics and Toxicology Centre

(AWTTC) personnel. The IR panel will only consider evidence already submitted – no new/additional evidence will be accepted at this late stage.

When and how are the decisions of the independent review (IR) panel communicated?
AWMSG will receive and consider the recommendations of the IR panel at a future meeting. AWMSG will remain the final arbiter of the IR in all cases.

What happens if an independent review (IR) is upheld?
If an IR is upheld a reappraisal by AWMSG will be undertaken.

What happens if an independent review (IR) is rejected?
If an IR is rejected, AWMSG's recommendation(s) to Welsh Government will become final and will be passed to Welsh Government for ratification. It is important to note that the role of AWMSG is to make *recommendations* to Welsh Government. It is Welsh Government who decides, on the basis of those recommendations, whether a medicine should be recommended for use by NHS Wales.

If the independent review (IR) is rejected, does the applicant company have any other course to challenge the decision?
There are two options: AWMSG may grant a re-appraisal if significant additional information becomes available, or the company may proceed to Judicial Review.

What happens if new data becomes available that would significantly impact on the decision that has been made?
The applicant company should inform the All Wales Therapeutics and Toxicology Centre (AWTTC) and the information will be taken by AWTTC to AWMSG for consideration and advice in relation to potential resubmission. AWMSG will advise on the course of action to be taken.

What is the status of the AWMSG recommendation whilst an independent review (IR) is being progressed?
The process is suspended pending the outcome of the IR and the final appraisal recommendation will not be forwarded to Welsh Government for ratification. NHS Wales will await final advice whilst the grounds of the IR are explored.

Updating of AWMSG advice

How regularly will the recommendations of AWMSG be reviewed?
Recommendations made after 1 October 2011 will be reviewed within three years of ratification by Welsh Government or in light of significant new information and on the production of any relevant National Institute for Health and Care Excellence (NICE) publications. In addition, recommendations may be reviewed if the actual budget impact is significantly different to that forecast within the submission. For negative or restricted positive recommendations the applicant company can resubmit at any time with significant new or additional information.