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Single Technology Appraisals by NICE
Are They Delivering Faster Guidance to the NHS?

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Abstract

**Background:** In 2005, a new technology appraisal process (the Single Technology Appraisal [STA]) was implemented by the National Institute for Health and Clinical Excellence (NICE), an independent agency that provides guidance to the UK NHS on the use of technology. The objective of STAs was to provide faster guidance to the NHS in order to help overcome the problems of 'NICE blight'.

**Methods:** Publicly available data from the NICE website and date of first marketing authorization (MA) from the Electronic Medicines Compendium were used to determine if STAs for cancer technologies have in fact been able to provide faster guidance than multiple technology appraisals (MTAs) for cancer interventions.

**Results:** STAs in cancer have, on average, taken 12.8 months from the date that NICE lists in the project history to guidance date. This compares with 20.7 months for MTAs in cancer. However, the time between the date of first MA and guidance is longer for cancer-related STAs than MTAs (95.1 months vs 74.6 months). The reasons for this are not clear; however, the STA programme includes examples of using an older product to treat a new cancer site, which may account for some of the differential. It may also reflect the timing that products are referred to NICE.

**Conclusions:** The overall results suggest that STAs may be faster once NICE looks at the specific product, but that there is a greater delay in the referral of STA products to NICE than for MTA products. However, the time taken for STAs is still short of the target of 9.75 months (or 39 weeks) [assuming no appeals].

**Background**

The speed of guidance issued by NICE has been raised as a concern and is often termed ‘NICE blight’. Manufacturers, clinicians and patients’ groups have all raised their concerns about the delay between product launch and availability of NICE guidance.[1-3] The UK’s Select Committee on Health has highlighted the following points:[6]

- clinicians may be prohibited by their primary care trust from prescribing a product until NICE guidance is available. This could, therefore, lead to geographical differences in access to certain products (often termed postcode prescribing);
- delayed guidance may harm patients who are waiting for treatment; and
- delays could mean that guidance, once available, is out of date.
Since November 2005, NICE has had two approaches to completing technology appraisals: MTAs and STAs.\(^7\) The STA process was explicitly introduced to allow NICE to provide guidance to the UK NHS more speedily than it had done previously. "The Single Technology Appraisal process is designed to enable comparison of single products, normally with single indications, with one or more standard treatment comparators. Both the STA and MTA processes can be initiated at any point in the life cycle of an intervention, but the assumption would be that the STA process would normally be used to ensure that NICE is able to issue guidance on new technologies, to the NHS, close to their point of introduction into the UK."\(^8\)

NICE MTAs take an average of 14 months, with STAs expected to take between 6 and 8 months.\(^9\)

### The STA Process

The NICE STA process includes a number of steps:\(^{10}\)

- Once the topic has been referred to NICE by the Secretary of State, NICE invites consultee and commentator groups to take part, and it will also issue the remit and scope of the appraisal.
- The manufacturer(s) will then put together evidence on their product(s) including communication with NICE to clarify any issues.
- The evidence from manufacturer(s) and any other parties will be considered by an evidence review group.
- The evidence review group will then produce a report, which is sent to the NICE appraisal committee for their consideration.
- NICE will have a pre-meeting to discuss the evidence before the NICE appraisal committee meets and hears statements from other parties (such as clinical experts, patient groups). This process is not expected to exceed 39 weeks if no appeal is lodged. Key stages in this timeline are as follows:\(^{10}\)
  - Week 0: Manufacturers’ evidence requested and consultee statements invited.
  - Week 9: Manufacturers’ evidence and consultee statements provided to NICE.
- Week 11: Clarification (if required) from NICE to manufacturer(s).
- Week 17: Evidence review group report provided to NICE.
- Week 19: Evidence review group report sent to NICE appraisal committee.
- Week 24: An appraisal consultation document is published and comments invited (alternatively, a final appraisal document may be produced, with 15 days for parties to appeal).
- Week 29: NICE appraisal committee meets.
- Week 34: NICE’s decision is communicated.
- Week 39: Final appraisal determination is published setting out NICE guidance.

The most important difference between the STA and MTA processes is the change to focusing on the manufacturer’s submission on the costs and benefits of their product, with the independent academic centre assessing the modelling and data provided by the manufacturer as opposed to developing a model and preparing an assessment report themselves.\(^9\)

This article reviews publicly available information from the National Institute for Health and Clinical Excellence (NICE) website to assess the speed of single technology appraisals (STAs) compared with multiple technology appraisals (MTAs). It focuses upon STAs in cancer, reflecting the focus of STAs completed to date (as at June 2008, 2.5 years after the implementation of STAs).

### Methods

This article uses publicly available data from the NICE website.\(^{11}\) NICE now routinely publishes a variety of information on each technology appraisal (whether MTA or STA), and this includes the following:

- a summary of their guidance
- the date issued
- the date due to be considered for review
- reference documents
- support for implementation and
development history, which includes the process (STA or MTA), topic area, NICE project team,
provisional schedule, stakeholders, project history and key documents.

This article uses data on all technology appraisals designated as STAs or MTAs in the cancer topic area. It has collated the summary of guidance, and the project history. The project history is used to determine a ‘start date’ for beginning the appraisal, and the issue date as the ‘finish date’ for completion of the appraisal. This is imperfect, as it is likely that the start date is earlier than the date provided on the NICE website; however, if this start date is equally imperfect across both STAs and MTAs, it is still possible to determine whether STAs are leading to faster guidance to the NHS than MTAs.

However, it does not provide a definitive answer as to whether guidance is becoming available closer to launch. Additional data taken from the Electronic Medicines Compendium is used as a proxy for the launch date. The Electronic Medicines Compendium provides access to the date of first marketing authorization (MA) in the UK in Summaries of Product Characteristics (SPCs). This is likely to be when the product became available in the UK, as products are not able to be supplied without an MA and there are few incentives to delay launch after the issuing of an MA. This is an imperfect but publicly available source of these data.

Results

As at June 2008, NICE has completed 18 STAs, from a total of 143 technology appraisals (although note that some of these have been reviewed and subsumed into new technology appraisals). Thus STAs account for 13% of all technology appraisals.

Table I sets out details of the 18 STAs, including their reference number, therapeutic area, product, recommendation, and months taken between the date first mentioned in the project history and the date guidance was issued. It also includes the date of first MA and the issuing of guidance, and the total months between MA and guidance to the NHS. In one instance, there is a mismatch between the date of first MA and the date of guidance, where the project history date may actually come before the date of first MA. This may reflect a mistake in matching to a product (the generic name was used to match against, but it is possible that a different formulation could account for the timing differential) or the start of the NICE appraisal process before the date of first MA.

The average time taken between the date first mentioned on the project history and the guidance date is 16.0 months for all STAs completed as at June 2008. This is longer than the average for MTAs reported by the OFT in 2007. However, this includes the time for technology appraisals that were moved from MTA to STA during the appraisal, and this is likely to have skewed the average time taken. Solely focusing on cancer-related STAs, the average time taken is reduced to 12.8 months.

The average time taken from the date of the first MA is much longer: 83.4 months for all STAs, and 95.1 months for cancer-related STAs (excluding the one instance in which the date of first MA occurs after the date of guidance and a review of a previous appraisal).

In order to determine if STAs are faster than MTAs, the same data were extracted for MTAs that focused on cancer. The focus is on cancer because cancer is also the focus of STAs published to date. Table II provides the same overview of MTAs in the cancer therapeutic area as in table I for STAs.

The average time between the date first mentioned on the project history and the guidance date is 20.7 months compared with 12.8 months for cancer-related STAs. This is longer than the average for all MTAs (14 months), and may reflect the focus on cancer. The reasons for the longer time period for cancer-related MTAs are not explored here but they may reflect a variety of reasons stemming from the complexity of the technology, the amount of data and information available and provided to inform the appraisal, and whether or not appeals occur.

1 Recommendations are summarized in line with the approach taken by the Office of Fair Trading (OFT), where recommendations are classified as either recommended with no restrictions and therefore recommended for general use, recommended with restrictions or not recommended.
<table>
<thead>
<tr>
<th>Therapeutic area and reference</th>
<th>Recommendation</th>
<th>First month mentioned in project history</th>
<th>Date issued</th>
<th>Monthsa to guidance</th>
<th>Date of first MA</th>
<th>Months from first MA to guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>TA109</td>
<td>No restrictions</td>
<td>Nov 05</td>
<td>Sep 06</td>
<td>10</td>
<td>Nov 95</td>
<td>130</td>
</tr>
<tr>
<td>TA108</td>
<td>Not recommended</td>
<td>Dec 05</td>
<td>Sep 06</td>
<td>9</td>
<td>Nov 93</td>
<td>154</td>
</tr>
<tr>
<td>TA107</td>
<td>Restrictions</td>
<td>Dec 05</td>
<td>Aug 06</td>
<td>8</td>
<td>Aug 00</td>
<td>72</td>
</tr>
<tr>
<td>TA116</td>
<td>Restricted</td>
<td>Mar 06</td>
<td>Jan 07</td>
<td>10</td>
<td>Oct 95</td>
<td>135</td>
</tr>
<tr>
<td>TA140</td>
<td>Not recommended</td>
<td>Mar 07</td>
<td>Apr 08</td>
<td>13</td>
<td>Aug 99</td>
<td>92</td>
</tr>
<tr>
<td>TA119</td>
<td>Not recommended</td>
<td>Sep 05</td>
<td>Feb 07</td>
<td>17</td>
<td>May 08</td>
<td>23</td>
</tr>
<tr>
<td>TA124</td>
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<td>Apr 06</td>
<td>Aug 07</td>
<td>16</td>
<td>Sep 04</td>
<td>23</td>
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<tr>
<td>TA137 (R)</td>
<td>Restrictions</td>
<td>Jan 07</td>
<td>Feb 08</td>
<td>13</td>
<td>Jun 98</td>
<td>116</td>
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<tr>
<td>TA129</td>
<td>Restrictions</td>
<td>Dec 05</td>
<td>Oct 07</td>
<td>22</td>
<td>Apr 04</td>
<td>30</td>
</tr>
<tr>
<td>TA110</td>
<td>No restrictions</td>
<td>Nov 05</td>
<td>Sep 06</td>
<td>10</td>
<td>Jun 98</td>
<td>87</td>
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<tr>
<td><strong>Asthma</strong></td>
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<tr>
<td>TA133</td>
<td>Restrictions</td>
<td>Mar 04</td>
<td>Nov 07</td>
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<td>Oct 05</td>
<td>25</td>
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<td><strong>Cardiovascular</strong></td>
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<td></td>
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<tr>
<td>TA122</td>
<td>No restrictions</td>
<td>Aug 06</td>
<td>Jun 07</td>
<td>10</td>
<td>Oct 88</td>
<td>224</td>
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<td><strong>Central nervous system</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>TA127 (T)</td>
<td>No restrictions</td>
<td>Aug 04</td>
<td>Aug 07</td>
<td>36</td>
<td>Jun 06</td>
<td>14</td>
</tr>
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<td><strong>Skin</strong></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA134 (T)</td>
<td>Restrictions</td>
<td>Aug 06</td>
<td>Jan 08</td>
<td>17</td>
<td>Aug 99</td>
<td>101</td>
</tr>
<tr>
<td>TA125</td>
<td>Restrictions</td>
<td>Aug 06</td>
<td>Aug 07</td>
<td>12</td>
<td>Sep 03</td>
<td>47</td>
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<td><strong>Musculoskeletal</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA141</td>
<td>Not recommended</td>
<td>Aug 06</td>
<td>Apr 08</td>
<td>20</td>
<td>Jul 07</td>
<td>9</td>
</tr>
<tr>
<td>TA126</td>
<td>Restrictions</td>
<td>Aug 06</td>
<td>Aug 07</td>
<td>12</td>
<td>Jun 98</td>
<td>110</td>
</tr>
<tr>
<td><strong>Mental health and behavioural problems</strong></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA123</td>
<td>No restrictions</td>
<td>Aug 06</td>
<td>Jul 07</td>
<td>11</td>
<td>Sep 06</td>
<td>10</td>
</tr>
</tbody>
</table>

a From first date mentioned in history.

b Inconsistency between date of first MA and date of guidance. Date of first MA comes after date of guidance.

MA = marketing authorization; R = review of appraisal; T = transferred to STA from multiple technology appraisal in August 2006.
### Table II. Published multiple technology appraisals (MTAs) in the cancer therapeutic area (as of June 2008)

<table>
<thead>
<tr>
<th>Reference and project</th>
<th>Recommendation</th>
<th>First month mentioned in project history</th>
<th>Date guidance issued</th>
<th>Months* to guidance</th>
<th>Technology</th>
<th>Date of first MA</th>
<th>Months from first MA to guidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>TA23: temozolomide for recurrent malignant glioma (brain cancer)</td>
<td>Restrictions</td>
<td>NA</td>
<td>Apr 01</td>
<td>Jan 99</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA112: hormonal therapies for adjuvant tx of early estrogen-receptor-positive breast cancer</td>
<td>No restrictions</td>
<td>Jul 03</td>
<td>Nov 06</td>
<td>40</td>
<td>Anastrozole</td>
<td>Jun 00</td>
<td>77</td>
</tr>
<tr>
<td>TA118: bevacizumab and cetuximab for metastatic colorectal cancer</td>
<td>Not recommended</td>
<td>Aug 04</td>
<td>Jan 07</td>
<td>29</td>
<td>Bevacizumab</td>
<td>Jan 05</td>
<td>24</td>
</tr>
<tr>
<td>TA61: capecitabine and tegafur uracil for metastatic colorectal cancer</td>
<td>No restrictions</td>
<td>May 02</td>
<td>May 03</td>
<td>12</td>
<td>Capcitabine</td>
<td>Feb 01</td>
<td>27</td>
</tr>
<tr>
<td>TA70: leukaemia (chronic myeloid) – imatinib</td>
<td>No restrictions</td>
<td>Sep 02</td>
<td>Oct 03</td>
<td>13</td>
<td></td>
<td>Nov 03</td>
<td>22</td>
</tr>
<tr>
<td>TA135: pemetrexed disodium for mesothelioma</td>
<td>Restrictions</td>
<td>Aug 04</td>
<td>Jan 08</td>
<td>41</td>
<td></td>
<td>Sep 04</td>
<td>40</td>
</tr>
<tr>
<td>TA65: rituximab for aggressive non-Hodgkin’s lymphoma</td>
<td>No restrictions</td>
<td>Oct 02</td>
<td>Sep 03</td>
<td>11</td>
<td></td>
<td>Jun 98</td>
<td>63</td>
</tr>
<tr>
<td>TA91 (R): topotecan, pegylated liposomal doxorubicin hydrochloride and paclitaxel for advanced ovarian cancer</td>
<td>Restrictions</td>
<td>Mar 04</td>
<td>May 05</td>
<td>14</td>
<td>Topotecan</td>
<td>Nov 96</td>
<td>102</td>
</tr>
<tr>
<td>TA55: review of clinical and cost effectiveness of paclitaxel for ovarian cancer</td>
<td>No restrictions</td>
<td>Sep 01</td>
<td>Jul 03</td>
<td>22</td>
<td></td>
<td>Nov 93</td>
<td>138</td>
</tr>
<tr>
<td>TA101: docetaxel for the treatment of hormone-refractory prostate cancer</td>
<td>Restrictions</td>
<td>Aug 04</td>
<td>Jun 06</td>
<td>22</td>
<td></td>
<td>Nov 95</td>
<td>127</td>
</tr>
</tbody>
</table>

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*a* From first date mentioned in history.

*b* Inconsistency between date of first MA and date of guidance. Date of first MA comes after date of guidance. Separate MA dates are provided for separate products.

**MA** = marketing authorization; **NA** = not applicable; **R** = review of appraisal; **tx** = treatment.
Once again, the average time taken from the date of the first MA is much longer (74.6 vs 95.1 months for cancer-related MTAs and STAs, respectively). The 74.6 months includes separate calculations for the date of first MA for each product included within the MTA, and excludes the one instance in which the date of first MA occurred after the date of guidance. This is substantially shorter than the average for STAs. The reasons for this are not clear; however, the STA programme includes examples of using an older product to treat a new cancer site, which may account for some of the differential. It may also reflect the timing that products are referred to NICE because NICE does not determine this itself, but rather looks at products selected by the Department of Health or other Government departments in the UK.

Conclusions

This simple analysis suggests that STAs are being completed faster than MTAs when the start date is based on NICE’s own project history. Based on a simple comparison of time taken between the date first mentioned on the project history and publication date, MTAs take 8 months longer than STAs. However, STAs are still taking a relatively long time to complete, and certainly more than the target (assuming no appeals) of 9.75 months (39 weeks). The picture is more complex when considering the date of first MA as a proxy for launch date. For cancer-related appraisals, STAs may actually take longer. This may in part reflect the move to STAs from existing MTAs, and STAs for older products for new cancer sites. It may also reflect poor data and potential mismatching of products. In general, it appears that once NICE begins an STA it is faster, but it may take longer for the product to be referred to NICE, thus making the total time between first MA and guidance date longer for STAs than for MTAs.

There is an inevitable tension between providing fast guidance to the NHS based on limited data, and slower guidance to the NHS based on more data as the product is used in practice. This author does not wish to specify an appropriate target, but highlights that NICE is not currently achieving policy maker’s own standards. However, the author does recommend that the time taken is monitored and regularly reported on and causes of delay are explored in order to determine what actions could be taken to improve the speed of guidance, within the overarching constraint of producing high-quality guidance.

This analysis has not been able to determine if STAs enable guidance to be issued to the NHS closer to launch (although this is likely to be the case) because data on the date of launch has not been reviewed. Proxy data on date of first MA have been used instead. Using actual launch dates would be a useful addition to determine if the objective for STAs has been achieved. Actual launch data are likely to be most reliably obtained direct from manufacturers.

This article has not explored the appropriateness of recommendations reached by either STAs or MTAs, nor has it explored whether implementation may differ between the two appraisal approaches.

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References


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