**SUPPLEMENTARY TABLE 1: HTA Guidelines on Medical Devices**

|  | **NICE-Medical Technologies**(7) | **NICE-Diagnostic Assessment Programme**(6) | **EUNetHTA- Medical Devices**(8) | **MSAC-Therapeutic**(9) | **MedTecHTA**(11)  | **HQO HTA Methods and Process Guidelines**(10) |
| --- | --- | --- | --- | --- | --- | --- |
| **Country of Publication** | UK | UK | Europe | Australia | Europe | Ontario, Canada |
| **Publication Year** | 2011 | 2011 | 2015 | 2016 | 2017 | 2018 |
| **Scope of Guideline (i.e., type of health technology included)** | Medical device, active medical device, active implantable medical device, in vitro diagnostic medical device. | Medical device, active medical device, active implantable medical device, in vitro diagnostic medical device. However, DAP concentrates more on pathological tests, imaging, endoscopy, algorithms or test combinations and physiological measurements. | Therapeutic medical device | Therapeutic medical service and investigative medical service  | Medical devices | Includes, but is not limited to, medical devices, medical tests, surgical procedures, health care programs, and complex health system interventions, including models of health care delivery. |
| **Product Life Cycle** | See Clinical Evaluation and Costs and Economic Evaluation |
| **Clinical Evaluation**  | Clinical evaluation can include published and unpublished evidence. Evidence may relate to primary clinical research (e.g., RCTs) or secondary research (such as evidence synthesis or modelling studies). Contributions from expert advisors related to their opinions on the published evidence and supplemental information relevant to the technology are also accepted. | Clinical evaluation can include published and unpublished evidence. Evidence may relate to primary clinical research (e.g., RCTs) and secondary research (high-quality systematic review, high-quality existing models). Moreover, more attention is focused on diagnostic test accuracy studies, long-term studies (RTC's and other comparative studies). Contributions from expert advisors related to their opinions on the published evidence and supplemental information relevant to the technology are also accepted. | Clinical evaluation can include published and unpublished evidence. Evidence may relate to primary clinical research (e.g., RCTs) or secondary research (such as evidence synthesis, clinical trial registers, modelling studies). Contribution from experts and patients may be valuable source of information. However, RCTs are preferred, but HTA assessors should anticipate that such evidence is frequently lacking for medical device interventions. HTA assessors should also be familiar with special RCT designs that take into account the specifics of medical devices.  | Clinical evaluation based on RCTs is preferred. However, clinical evidence can include published and unpublished evidence. Evidence may relate to primary clinical research or secondary research (such as evidence synthesis, clinical trial registers, modelling studies). Contributions from expert advisors related to their opinions on the published evidence and supplemental information relevant to the technology are also accepted. | Clinical evaluation can include published evidence. Evidence may relate to primary clinical research (e.g., RCTs) or secondary research (such as evidence synthesis, disease-based or device based registers).  | Clinical evaluation can include evidence from the published and grey (i.e., literature that is not commercially available) literature. Contribution from content experts is also accepted. Clinical evidence review systematically identifies, synthesizes, and analyses relevant clinical evidence to provide an assessment of the clinical benefits and harms of the health technology.  |
| Depending on the size and quality of the evidence base, evidence synthesis or meta-analysis may be used to summarize evidence from different studies and to measure uncertainty and undertake sensitivity analysis.  | Depending on the size and quality of the evidence base, evidence synthesis or meta-analysis may be used to summarize evidence from different studies and to measure uncertainty and undertake sensitivity analysis. Other type of meta-analysis could be performed: meta-analysis of likehood ratios and predictive values, meta-analysis of diagnostic odds ratio, Moses-Littenberg summary ROC curves, and hierarchical models. The choice of meta-analysis is a trade-off.  | Depending on the size and quality of the evidence base, evidence synthesis or meta-analysis may be used to summarize evidence from different studies and to measure uncertainty and undertake sensitivity analysis. Other analysis such as subgroup analysis, sophisticated statistical approaches and meta-regression can be provided if applicable. Need for specific methods: incremental development of medical devices, user and context dependence, and some implications of the physical mode.  | Depending on the size and quality of the evidence base, evidence synthesis or meta-analysis may be used to summarize evidence from different studies and to measure uncertainty and undertake sensitivity analysis. Other analysis such as subgroup analysis or a meta-regression can be provided if applicable.Moreover, statistical analysis of variation of the comparative treatment effect, elicitation and interpretation of scenario-based utility valuation of health outcomes are also performed.  | Appropriate methods for confounder adjustment in comparative effectiveness or safety analyses and try to address residual confounding.If data from large registries are included in evidence synthesis, consider bias-adjustment based on expert elicitation as one scenario in the sensitivity analysis. | Depending on the size and quality of the evidence base, evidence synthesis, statistical analysis or meta-analysis may be used to summarize evidence from different studies and to measure uncertainty and undertake sensitivity analysis.  |
| **User Issues** | Not reported.  | In some cases, the scopes identify special implementation issues and recommendations for use of a diagnostic test (the training and skills of those providing the test, availability of equipment, and the availability of other portions of the care pathway). | Not reported. | Not reported. | Not reported. | The adoption of the health technology into Ontario’s health system is also discussed in terms of assessing the impact of adopting the service or device on the currently available health care resources, as well as any resource gaps that would need to be addressed or system-level changes (e.g., fee schedule changes) that would need to be made for the health technology to be successfully adopted.  |
| **Costs and Economic Evaluation** | Consideration of the costs of the technology, including initial acquisition costs (including associated infrastructure) and running costs (including maintenance and consumables).Cost-consequence models are in scope and should capture and quantify the impact of introducing a new technology into the current healthcare pathways and routine NHS use. Discounting principles and uncertainty techniques are applicable. | Consideration of the costs of the technology, including initial acquisition costs (including associated infrastructure), running costs (including maintenance and consumables) and also costs resulting from treatments after use of a diagnostic treatments.  Cost-effectiveness Analysis (cost-utility) is the preferred form of economic evaluation. This seeks to establish whether differences in costs between options can be justified in terms of health effects related to quality of life. Health-related quality of life changes should be expressed in terms of QALYs. Discounting principles and uncertainty techniques are applicable.  | Cost-effectiveness will not be discussed, nor will other non-clinical benefits and harms (e.g., system/ organisation benefits/harms) due to limited time resources.  | Consideration of the costs of the technology, including initial acquisition costs (including associated infrastructure) and running costs (including maintenance and consumables). Review the relevant economic literature is conducted. As primary evaluation cost-effectiveness analysis and Cost-utility analysis are preferred. The denominator in a cost-utility analysis is most commonly theincremental QALY. Extensive sensitive analyses are also performed to examine the effect of uncertainty aroundestimates and assumptions included in the economic evaluation on the results of the base-caseeconomic evaluation. Whereas a cost-benefit analysis is a supplementary option and cost-consequences analysis is considered if disaggregation of outcomes would be helpful. Discounting principles and uncertainty techniques are applicable.  | Economic evaluations should pay attention to the particular characteristics of medical devices and explore their quantitative impact on cost-effectiveness.Recommend consideration of iterative process to the medical device evaluation as additional evidence and learning emerges over time, as well as the likelihood of price changes.  | A systematic review is conducted to summarize the evidence from all relevant economic studies that have been published on the health technology. When appropriate, a primary economic evaluation is conducted to determine the cost-effectiveness of the health technology compared with its alternatives. Consideration of cost of technology (e.g., device cost, treatment cost, adverse events), treatment administration is also considered. The economic evaluation typically uses quality-adjusted life year. Discounting principles and uncertainty techniques are applicable. Finally, the potential budget impact of publicly funding the new health technology in Ontario is presented. |
| **Intellectual property** | See Costs and Economic Evaluation |

DAP = Diagnostic assessment programme; EUnetHTA = European Network for Health Technology Assessment; HQO = Health Quality Ontario; HTA = Health technology assessment; MedTecHTA= Methods for Health Technology Assessment of Medical Devices; MD = medical devices; MSAC = Medical Services Advisory Committee; NHS = National Health Service; NICE = National Institute for Health and Clinical Excellence; QALYs = quality adjusted life-years; RCT = randomized controlled trial.

# **SUPPLEMENTARY FILE 1: Modified Delphi Survey**

# SECTION ONE - ABOUT YOU, YOUR ROLE, YOUR ORGANISATION

## Personal info

### Q1 Do you consider yourself a:

* Clinical Engineer
* Clinical Technologist or technician
* Biomedical Engineer
* Biomedical Engineer
* Healthcare Technologist or Technician
* Research Scientist
* Manager
* Other – please specify

### Q2 What is your highest level of education obtained?

* BSc
* MSc
* PhD
* Other – please specify

### Q3 Years of service (please select one option):

* 1-5 years
* 6-10 years
* 11-15 years
* 16+ years

## Your role/organization

### Q4 Which of the following best describes your role (select all that apply)?

* Healthcare Technology Research
* Healthcare Technology Innovation
* Healthcare Technology Applications
* Healthcare Technology Management
* Healthcare Technology Maintenance
* Healthcare Technology Service
* Healthcare Technology Selling
* Healthcare Technology Assessment
* Other – please specify

### Q5 What type of organisation is your principal employer (select one)?

* Healthcare Provider – acute hospital
* Healthcare Provider – community care
* Academic institution (university)
* Academic institution (other research group)
* Industry/Commercial – manufacturer
* Industry/commercial – supplier
* Industry/commercial – services
* Other – please specify

### Q6 In which country are you based (select one option):

* [Drop down list of countries]

# SECTION TWO- DELPHI SURVEY

## Product Lifecycle

### Q7 Medical device innovation is rapid and incremental. Moreover, medical devices have a short lifecycle compared with drugs.

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* The timeframe to perform a complete a HTA is much reduced in the medical device lifecycle compare to drugs. Spending several months or years to conduct a HTA may result in an outdated or obsolete (e.g., a newer version of the device is available) report.
* Limited evidence is available to meet the objectives of HTA
* The time horizon of the economic evaluation may be inaccurate
* Estimates of cost recovery may be inaccurate in the cost-effectiveness analyses
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Use the available evidence to accurately estimate the cost-effectiveness of the medical device and to quantify its uncertainty. When evidence is lacking, HTA experts could run clinical performance and usability analysis to gather relevant insights for their analysis.
 | 1 | 2 | 3 | 4 | 5 |
| * Use appropriate methods to assess the quality of modelling the effect of the different types of evidence on the effectiveness and safety of the medical device
 | 1 | 2 | 3 | 4 | 5 |
| * Conduct sensitivity analyses in economic model to measure the impact on the results of varying lifespans or incremental innovations
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

### Q8 Maintenance and servicing are required with medical devices but considerably less so with drugs

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* Maintenance of the device and the characteristics of the services for the device may impact costs, efficacy, effectiveness, and safety of the medical device over its lifespan.
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Obtain additional insights about the maintenance required, and capture maintenance impact in the HTA by using appropriate methods of contextual inquiry. The context inquiry can include, for instance, gather information about the service requirements in terms of preventive maintenance planning, costs, downtime and by gathering qualitative data about the needs of the stakeholders of the service.
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

### Q9 Individual parts of the medical device (e.g., software, spare parts), may have even shorter lifecycle, while drugs compounds last longer than the entire drug

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* Instability of individual parts may impact the safety, efficacy, effectiveness, user satisfaction, and costs
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* + Conduct a risk assessment by using appropriate and validated tool or standards
 | 1 | 2 | 3 | 4 | 5 |
| * + Conduct, when necessary, a simulation of use to empirically analyze safety in use and define procedures of risk report, and processes to mitigate residual risks
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

### Q10 As explicitly stated in the WHO definition, medical devices can be used alone or in combination with other technologies. There are many interdependences (e.g., among differed medical devices or between a medical device and its operational environment), which may affect their safety, efficacy, effectiveness, costs and economic evaluation.

|  |
| --- |
| Gaps in HTA Medical Device Guidelines: The majority of HTA studies focuses one technology per time and dependences of this technology with surrounding ones are almost never considered* In the majority of high-income countries, minimum requirements in terms of organization (e.g. personnel), technology (e.g. plants, isolation) and structure (e.g. physical spaces) are explicitly defined, in accordance with international standards, and represent a necessary condition to be authorized to offer healthcare services. These minimum requirements are assumed as granted when designing medical devices (e.g., equipotential node and isolation transformer in surgical theatres). Any deviation from the minimum requirements may negatively impact the safety, efficacy, effectiveness, and costs of the medical device; thus, reducing the generalization and transferability of HTA results.
* HTAs are based on the highest available evidence and efficacy is mainly evaluated with RCTs of the device, if feasible. These trials are performed in environments (e.g., university hospitals, specialized wards, etc.), which have much higher standard than those defined by the national minimum requirements (e.g., more specialized personnel, better equipment, etc.)
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Map the process of device use, and explicitly state the organizational constraints, technological and structural conditions in which the trial was performed
 | 1 | 2 | 3 | 4 | 5 |
| * Conduct an analytic assessment to estimate “what if” the minimum requirements are not met
 | 1 | 2 | 3 | 4 | 5 |
| * Manage and ensure processes of data exchange and interoperability of the device with hospital system and with other devices
 | 1 | 2 | 3 | 4 | 5 |
| * Increase stakeholders (i.e., technicians, health care providers, and patients) awareness of interdependences and interferences among the devices
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

## Clinical Evaluation

### Q11 There is a longer learning curve associated with the use of medical devices compared with drug therapies.

|  |
| --- |
| Gaps in HTA Medical Device Guidelines: Impact on the estimation of efficacy, effectiveness, satisfaction in use, cost-effectiveness, service provision  |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Use both pre-market and post-market studies to capture impact of learning curve on outcomes. The evidence can include a risk and usability assessment.
 | 1 | 2 | 3 | 4 | 5 |
| * Collect and report data on the effects of learning on relevant procedural and clinical outcomes during clinical trials, both at the physician and health care system levels
 | 1 | 2 | 3 | 4 | 5 |
| * Collect registry data that allow the estimation of the learning curve based on routine use of the medical device once it has been adopted in clinical practice
 | 1 | 2 | 3 | 4 | 5 |
| * Explicitly state the clinicians’ experience with the specific procedure (e.g., number of hernia repairs performed on similar patients) and in particular with the device under assessment of a similar one (e.g., previous version, similar device), if any
 | 1 | 2 | 3 | 4 | 5 |
| * Describe in detail the training and training materials for the device use (e.g., guideline of use and service process associated to the device use, etc.) provided to the users of the medical device
 | 1 | 2 | 3 | 4 | 5 |
| * Use appropriate statistical methods to incorporate learning curve corrections into the measurement of costs and relevant outcomes
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

### Q12 Designing a randomised control trial (RCT) for a medical device is more challenging than for drugs

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* Blinding is a challenge in a study with medical devices.
* Unlike drugs, medical devices are diagnostic and therapeutic, and they can influence the clinical decision making process and the patient’s clinical care pathway.
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Adopt appropriate study designs for medical devices. The design can include preliminary phases of clinical pathway mapping and qualitative analysis to identify the most appropriated setting, comparators and variables to be considered in a trial.
 | 1 | 2 | 3 | 4 | 5 |
| * Reinforce the use of simulation (e.g., in silico trial) in case of incremental innovation
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

## Issues in Use

### Q13 Performance of a medical device is strongly dependent on user, much more than drugs

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:The same medical device used by different users in different contexts may have different costs, efficacy, effectiveness, and safety, both in the short time (e.g., during the trial) and during its lifespan.  |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Use both pre-market and post-market data to capture impact of context of use variables (i.e., user, tasks, physical and social environment) on HTA outcomes
 | 1 | 2 | 3 | 4 | 5 |
| * Simulate and use appropriate statistical methods to analyze the different types of evidence on the effectiveness and safety of the medical device
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

### Q14 Medical devices can require intensive training prior to use in clinical practice

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* The required training may impact costs, efficacy, effectiveness, and safety of the medical device.
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Use both pre-market and post-market studies to capture impact of learning curve on outcomes
 | 1 | 2 | 3 | 4 | 5 |
| * Select appropriate outcomes that reflect impact of the learning curve and the setting in which the device will be operated
 | 1 | 2 | 3 | 4 | 5 |
| * Simulate and use appropriate statistical methods to analyze the different types of evidence on the effectiveness and safety of the medical device
 | 1 | 2 | 3 | 4 | 5 |
| * Perform training simulations to help develop appropriate training strategies for the users
 | 1 | 2 | 3 | 4 | 5 |
| * Use appropriate statistical methods to to analyze the different types of evidence that reflects the learning curve with the medical device
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

## Costs and economic evaluations

### Q15 Maintenance, installation, and ongoing operational costs

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* Impact on cost-effectiveness and budget impact.
* There is a lack of evidence-based maintenance and service program formulation, manufacturer recommendations can be difficult to fulfill in budget-constrain circumstances and this can cause safety problems or affect medical device effectiveness along the whole lifecycle.
* Maintenance and installation procedures, and therefore their costs per each device, depend strongly on local clinical engineering and biomedical technician availability and expertise. This change significantly costs across different hospitals.
 |
| * Recommendations to Address Gaps in HTA Medical Device Guidelines: Understand and describe explicitly in the HTA report, all the possible maintenance, installation, and operational costs considered
 | 1 | 2 | 3 | 4 | 5 |
| * Ensure that all reasonable maintenance, installation, and ongoing facilities costs are incorporated in the economic evaluation, or explicitly state the hypothesis of the study conducted
 | 1 | 2 | 3 | 4 | 5 |
| * Describe the organizational model considered in the economic evaluation for maintenance and installation (e.g., internal clinical engineering service)
 | 1 | 2 | 3 | 4 | 5 |
| * If possible, ensure that costs arising from missed maintenance are considered, too
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree

### Q16 Different financial models of acquisition of the technology (e.g., leasing) – scarce use of risk sharing agreements

|  |
| --- |
| Gaps in HTA Medical Device Guidelines:* Impact on cost-effectiveness and budget impact
 |
| Recommendations to Address Gaps in HTA Medical Device Guidelines:* Understand and ensure that the potential impact of financial models are represented in the economic evaluation
 | 1 | 2 | 3 | 4 | 5 |
| Comments/suggestions: |

 1 = Strongly disagree; 2 = Disagree; 3 = Neither agree nor disagree; 4 = Agree; 5 = Strongly agree