MANUFACTURER SUBMISSION TEMPLATES TO SUPPORT PRODUCTION OF CORE HEALTH TECHNOLOGY ASSESSMENT (HTA) INFORMATION

EUnetHTA work package 7
subgroup 4

Objectives

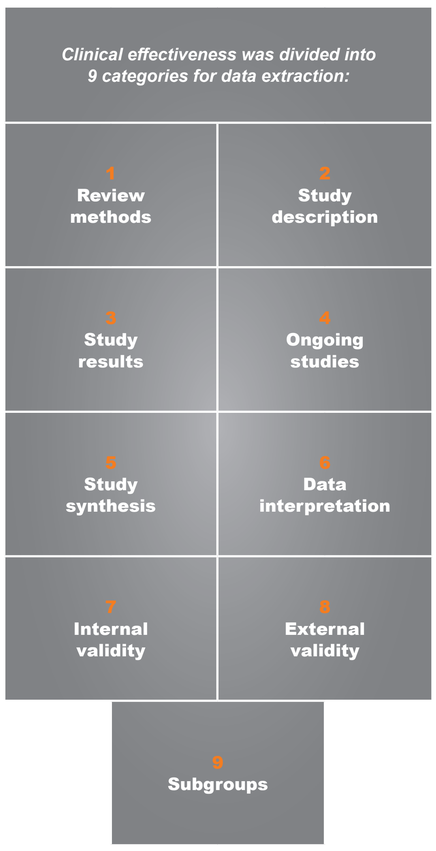
- Produce a manufacturer submission template that can be used by any national agency for HTA and reimbursement decisions, and where appropriate for joint assessments by multiple agencies
- Include evidence requirements of all national European reimbursement agencies relating to 'relative effectiveness assessment' (figure 1)
- Produce a flexible template so agencies can use the questions and modules relevant to their criteria for decision making

Figure 1: Domains of the HTA CORE model used in 'relative effectiveness assessment'

Methods

- National agencies involved in reimbursement were asked for their evidence requirements
- Using a framework (figure 2) based on the first 4 domains of the HTA CORE model, data were extracted from the evidence requirements into the framework by SG4 EUnetHTA partners*
- Data extractions were quality assured by a second SG4 EUnetHTA partner
- Final data extractions were analysed for similarities and differences in information requested by national agencies, and used to develop a template
- For each of the 4 HTA CORE model domains, questions were developed, then grouped into modules according to themes

Figure 2: Example of the data extraction framework for clinical effectiveness



*Agencies involved in the development of the submission template:

- Agenzia Nazionale per i Servizi Sanitari Regionali (AGENAS)
- Italian Medicines Agency (AIFA)
- Gemeinsamer Bundesausschuss (G-BA)
- National Institute for Quality and Organizational Development in Healthcare and Medicines (GYEMSZI)
- Healthcare Improvement Scotland (HIS)
- Ministry of Health Czech Republic
- National Institute for Health and Care Excellence (NICE)
- National Centre for Pharmacoeconomics (NCPE)
- Zorginstituut Nederland

Figure 3: Evidence requirements received from national agencies

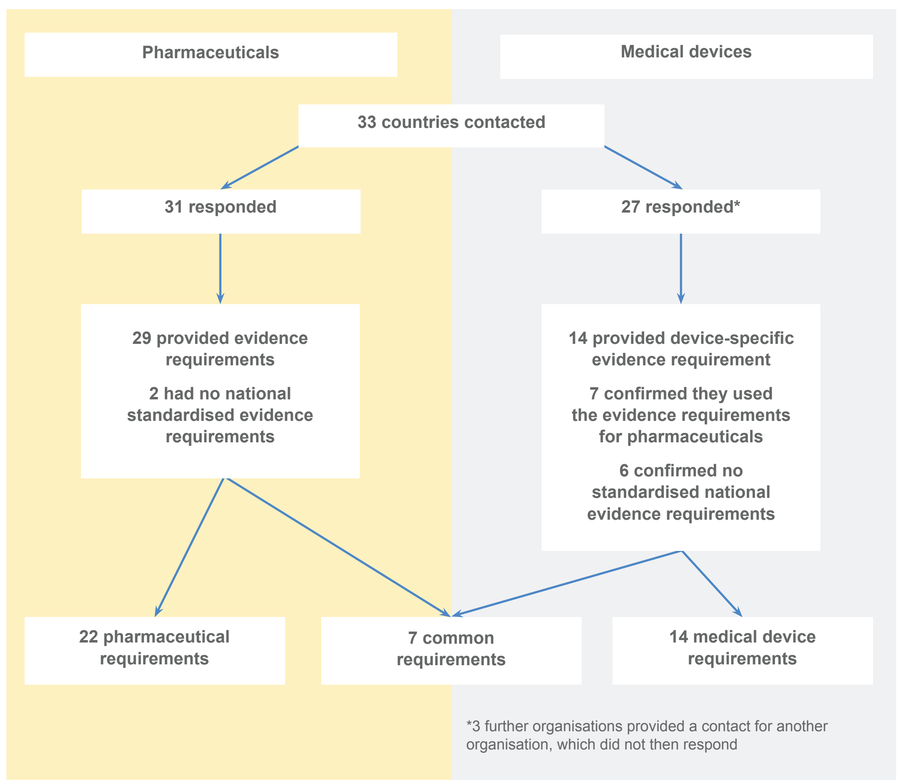
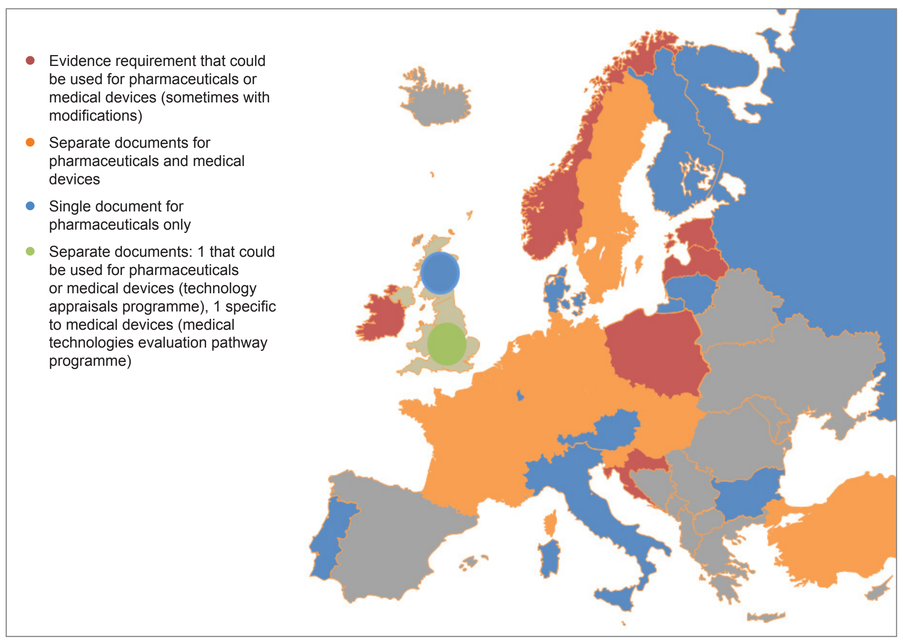


Figure 4: Evidence requirements provided by country



Results

29 countries provided 43 evidence requirements: 29 for pharmaceuticals and 21 for medical devices (figures 3 and 4). Documents included templates, checklists, methods guides and legal ordinances. The number of pages ranged from 3 to 170. All the evidence requirements asked for 1 or more pieces of information for each of the 4 domains.

Health problem and current use of the technology

- Evidence requirements were similar for medical devices and pharmaceuticals
- Information was organised into 4 modules with 19 questions (table 1)
- Most frequently requested information: disease description (65%), prevalence and incidence of the disease (56%), current clinical management (56%), proposed use (65%), identification of comparators (88%) and size of the target population (88%)

Description and technical characteristics of the technology

- Evidence requirements were different for medical devices and pharmaceuticals
- Information was organised into 5 modules for pharmaceuticals and 8 for medical devices (table 2). There are 40 questions for the medical device template and 20 for the pharmaceutical one
- Most frequently requested information: regulatory information in the country of application (100%), classification codes (80%, pharmaceuticals only), dosing and administration (93%, pharmaceuticals only), and reimbursement and/or pricing information in other countries (64%)

Clinical effectiveness and safety

- 32 evidence requirements asked for clinical effectiveness and safety information to be presented separately. Safety information presented separately was most frequently study results from individual studies (44%) and interpretation of the evidence relating to safety (40%)
- Evidence requirements were similar for medical devices and pharmaceuticals
- Information was organised into 13 modules for both pharmaceuticals and medical devices, 1 for medical devices only and 1 for pharmaceuticals only. There are 77 questions in the pharmaceutical template and 80 in the medical device one (table 3)
- Most frequently requested information: listing clinical evidence (84%), describing studies (65%), presenting study results (70%) and summarising conclusions from clinical evidence (79%)

Validation and next steps

Expert meetings were held with the European Federation of Pharmaceutical Industries and Associations, European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry, European Diagnostic Manufacturers Association and EUCOMED to discuss the templates. The first draft of the templates is being piloted in EUnetHTA relative effectiveness assessments and in a national process. A targeted consultation with national agencies and other stakeholders will take place from January 2015. Agencies will be asked to validate the information included in the data extraction for their agency and to comment on the draft template. Final templates will be available on the EUnetHTA website.

Structure of the draft manufacturer submission template

Table 1: HTA CORE model domain – description of health problem and current use of technology

Module title	Content of questions included in module	Use of module
1. Overview of the disease or health condition	Description of disease, causes or risk factors, natural course, prevalence and incidence, symptoms and burden to patients, consequences to society, aspects of burden targeted by technology	Modules used for both pharmaceuticals and medical devices
2. Current clinical management	Current clinical management, issues in management	
3. Target population	Description and justification, comparators and justification, size of population, pathway of care with new technology	
4. Current use of technology and comparators	Experience of using the new technology, scale of current use, scale of use of comparators, variations in use of comparators	

Table 2: HTA CORE model domain – description and technical characteristics of the technology

Module title	Content of questions included in module	Use of module
1. Feature of the technology and comparator	Names, active substance, galenic form, product codes, mechanism of action	Adapted for use with medical devices
2. Detailed characteristics	Description of the technology, diagram, how the technology is used, different models, package contents, history of development	Medical devices only
3. Administration and dosing	Packaging, volume in packaging, recommended course of treatment, dosing, posology	Pharmaceuticals only
4. Investments, personnel and tools required for use	Context and level of care, concomitant therapies, who administers treatment, infrastructure, supplies and equipment required	Used for both pharmaceuticals and medical devices
5. Regulatory information	Approval status, wording of indication, other available indications, date of approval, launch date, conditions attached to authorisation	Adapted for use with medical devices
6. Reimbursement information	Reimbursement status in Europe, indications, restrictions and levels of reimbursement, date of decision, summary of recommendations	Used for both pharmaceuticals and medical devices
7. Details of manufacture and follow up	Location of manufacture, distribution mechanism, availability of spares and replacements, maintenance requirements, quality control requirements and medical surveillance requirements, statistics of repairs	Medical devices only
8. Procedures required to use the device	Type of procedure and approach, technical platform, anaesthesia requirements, whether the device is required to complete the procedure, similarities and differences where more than one procedure may be used	Medical devices only
9. Duration of life, guarantees and warranties	Life of the device and component parts, details of guarantees and warranties	Medical devices only

Table 3: HTA CORE model domains – clinical effectiveness and safety

Module title	Content of questions included in module	Use of module
1. Identification and selection of studies	Research question, databases and registries, search dates, search strategies, inclusion and exclusion criteria, flow chart, methods for identifying ongoing and unpublished studies, citation hits	Used for both pharmaceuticals and medical devices
2. List of relevant studies	Study reference, registration name/number, conflicts of interest, study dates, study location, source of identification, references to linked publications, status	Used for both pharmaceuticals and medical devices
3. Details of the characteristics of studies	Study objective, design, population, intervention, comparator, follow up, primary and secondary outcome, randomisation methods, methods blinding, methods allocation concealments, methods of analysis	Used for both pharmaceuticals and medical devices
4. Individual study results for clinical effectiveness	Sample size determination, patient withdrawal, baseline comparison, study results (including assessment measure, time point, n with event, n without event, mean, standard deviation, difference, confidence interval, p value)	Used for both pharmaceuticals and medical devices
5. Individual study results for safety	Exposure, discontinuation and withdrawal of treatment, number of adverse events, susceptible patient groups	Used for both pharmaceuticals and medical devices
6. Risk of bias study level (randomised studies)	Randomisation sequence, allocation concealment, blinding, complete outcome reporting, other aspects of bias	Used for both pharmaceuticals and medical devices
7. Risk of bias study level (observational studies)	Determination of treatment group, baseline comparability, minimisation of bias, complete outcome reporting, intention to treat (ITT) implementation, other aspects of bias	Used for both pharmaceuticals and medical devices
8. Risk of bias outcome level	Blinding of outcome assessor, ITT implementation, complete outcome reporting, other aspects of bias	Used for both pharmaceuticals and medical devices
9. Methods of evidence synthesis	Type of synthesis, outcomes in synthesis, justifications, methods used for synthesis, heterogeneity, consistency, publication bias, sensitivity analyses	Used for both pharmaceuticals and medical devices
10. Conclusions on clinical effectiveness	Relative effects on mortality, morbidity, management, quality of life, satisfaction	Used for both pharmaceuticals and medical devices
11. Conclusions on safety	Harms (absolute and versus comparator), dose relationship, onset, changes over time, data on susceptible groups	Used for both pharmaceuticals and medical devices
12. Subgroups	Characteristics, justification, plausibility, analysis methods, results	Used for both pharmaceuticals and medical devices
13. Strengths and limitations	Internal validity, relevance of evidence base to scope, factors influencing external validity	Used for both pharmaceuticals and medical devices
14. Manufacturer vigilance data	List of incidents, corrective measures, recalls, modifications, methods of optimising or limiting service to minimise risk	Used for medical devices
15. Safety risk management	Methods of optimising or limiting service to minimise risk, changes to marketing authorisation as a result of safety, other harms appearing after granting of marketing authorisation	Used for pharmaceuticals

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