



## **Agency for Quality and Accreditation in Health Care, Croatia**

Department for Development, Research and Health Technology Assessment

# **The Croatian Guideline for Health Technology Assessment Process and Reporting**

**1<sup>st</sup> edition, February 2011**

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The Agency takes the full responsibility for the final form and content of this Guideline.

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## Foreword

This 1<sup>st</sup> edition of The Croatian Guideline for Health Technology Assessment Process and Reporting is based on, and accepted from, HTA Guidelines from National Institute for Health and Clinical Excellence (NICE), The Canadian Agency for Drugs and Technologies in Health (CADTH), Belgian Health Care Knowledge Centre (KCE), Danish Centre for Health Technology Assessment, and EUnetHTA Core Models (references are listed in Appendix I), with adaptation to Croatian setting. The part of this Guideline, Guide for Croatian primary health economic analysis, is solely accepted, and adapted, from NICE HTA Guidelines. The 1<sup>st</sup> edition was written in time when some limitations existed at national, as well at Agency level, primary because of recognized barriers such limited HTA legal framework, number of staff, and Agency funds. The Guideline will be updated according to necessary future changes in Croatian HTA legal framework, testing phase during the first pilot HTA process, and finished process of Agency and national HTA capacity building.

Whole HTA process in Croatia will be organized as “network”. Each HTA Report will be designated as ‘internal’, or ‘internal plus external’, depending upon the resources available. If part of HTA is designed ”external”, national as well as international academic and scientific institutions, Cochrane centers, and HTA Agencies or units or organization from EUnetHTA will be contacted for a contract of part of specific HTA project. To assist knowledge transfer, target audience for each report will be always indicated. A high-quality HTA Report should provide Croatian decision-makers with useful, relevant, and timely information. Agency, as legal person, takes whole responsibility for the whole process and final form and content of all Agency HTA reports.

The Croatian Guideline for Health Technology Assessment Process and Reporting is prepared by the Agency for Quality and Accreditation in Health Care, Zagreb, Croatia, Department for Development, Research and Health Technology Assessment, and members of independent multidisciplinary HTA Working Group, appointed by Agency for this purpose. Authors are listed below;

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associate to the Department for Development, Research and Health Technology Assessment (September 1 2010 - January 31 2011).

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### **Conflict of Interest**

Further authors declared no conflict of interest; *Mirjana Huić, Ana Bobinac, Prof. Ranka Štern Padovan, Prof. Marijan Klarica, Prof. Ana Marušić, Prof. Maja Vehovec, Pero Draganić, and Vatroslav Zovko.* Some contributors declared work conducted with the pharmaceutical industry, being aware of sensitivities regarding these relationships and in the interest of being completely transparent, and with the intent of contributing to the rigor of these guidelines namely: *Prof. Vera Vlahović Palčevski* declared speaking honoraria from AstraZeneca, travel funds from Pfizer and Pharma Swiss, and received research funding (Medical Faculty) from Roche, Sanofi Aventis and Krka Pharma. *Prof. Igor Francetić* declared several speaking honoraria from different companies (Pliva, Pfizer, Sanofi-Aventis and Novartis). *Prof. Dinko Vitezić* declared expert reports honoraria, educational symposia and clinical drug trials.

### **Reviewers**

The Guideline was completed in July 2010, and sent for international peer-review process. All comments that were received from reviewers were considered when

preparing the final version in February 2011. Not all can be incorporated due to the already mentioned barriers, but will be in mind for the next Guideline version.

Agency wishes to thank the following individuals for kindly providing comprehensive review of this Guideline, important for its quality assurance (in alphabetic order):

*Dr Charalabos-Markos Dintisios*, MPharm, Economist, MA, MPH, Institute for Quality and Efficiency in Health Care (IQWiG), Germany; *Andreas Gerber*, MD, PhD, MA, MSc, Institute for Quality and Efficiency in Health Care (IQWiG), Germany; *Dr Suzanne Hill*, World Health Organization (WHO); *Donald Husereau*, BSc Pharm, MSc, Canadian Agency for Drugs and Technologies in Health (CADTH), Canada; *Prof. Finn Kristensen*, MD, PhD, European network for Health Technology Assessment (EUnetHTA), National Board of Health, Denmark; *Prof. Carole Longson*, PhD, National Institute for Health and Clinical Excellence (NICE), United Kingdom; *Alric Ruether*, MD, PhD, Institute for Quality and Efficiency in Health Care (IQWiG), Germany.

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## I Introduction and legal framework

The Agency for Quality and Accreditation in Health Care was established in 2007 as a legal, public, independent, non-profit institution under the Act on Quality of Health Care (*Official gazette No. 107/2007*). According to this Act, the Agency should provide Health Technology Assessment and Database on HTA.

Responsible persons for HTA process and Report will be Agency's Assistant Director and Head of Department for Development, Research, and Health Technology Assessment (HTA).

HTA is a multidisciplinary process which summarizes information in a systematic, transparent, unbiased and robust manner about medical, social, economic and ethical issues related to the use of a health technology to inform the formulation of safe and effective health policies that are patient focused and seek to achieve best value.

Aim of Croatian HTA process and reporting is to produce credible and standardized information that is relevant and useful to decision makers in Croatian publicly funded health care system, and to meet their needs for reliable, consistent, timely and relevant HTA information.

Croatian HTA reports should serve *as recommendation*, with aims to support policy-makers at national level, particularly Croatian Ministry of Health and Social Welfare and Croatian Institute for Health Insurance, in making evidence-informed decisions on the strategic planning, investment, management and the implementation of technologies in health care, on funding (reimbursement) and coverage of health technologies, and, on hospital level, on requests from hospital directors and policy teams.

Health technologies referred to the Agency include: pharmaceuticals, medical devices, diagnostic and screening techniques, surgical procedures, other therapeutic technologies and procedures and health promotion activities.

HTA process should have the following main parts: Topics suggestion and selection process, definition of Scope for HTA, Assessment process, Advice (Appraisal) process, and Report preparing and publishing.

Currently, legal framework for HTA is limited, so part of HTA process, Advice (Appraisal) process, will be defined later in a new version of the Guideline (in case future changes in HTA legal framework stated that Appraisal process also belongs in Agency jurisdiction).

A Single Technology Assessment (STA) covers a single technology for a single indication. Whole process should be done in time frame of 3 months, specially if drugs and medical devices are assessed for reimbursement decisions and listing on Drug or Medical Devices Lists, when timelines from so called “Transparency Directive” should be respected (Council Directive 89/105/EEC of 21 December 1998 relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance system).

A Multiple Technology Assessment (MTA) will normally cover more than one technology, or one technology for more than one indication. Timeline for full process and report should be in time frame of 6 (maximum 9) months. This timeline will be tested within the initial pilot HTAs, and the timing of each phase of HTA process and reporting will be mapped out in next version of the Guideline, for greater understanding and meeting public expectations. Agency recognizes importance of timely production of information to fulfill decision-makers needs.

Full HTA report should have the following domains (according to the EUnetHTA documents: HTA Core Model for Medical and Surgical Interventions, HTA Core Model for Diagnostic Technologies, HTA Core Model for Screening Technologies):

1 Current use of the technology (implementation level), 2 Description and technical characteristics of technology, 3 Safety, 4 Effectiveness (including Accuracy for diagnostic and screening techniques), 5 Costs, economic evaluation, 6 Ethical aspects, 7 Organizational aspects, 8 Social aspects and 9 Legal aspects.

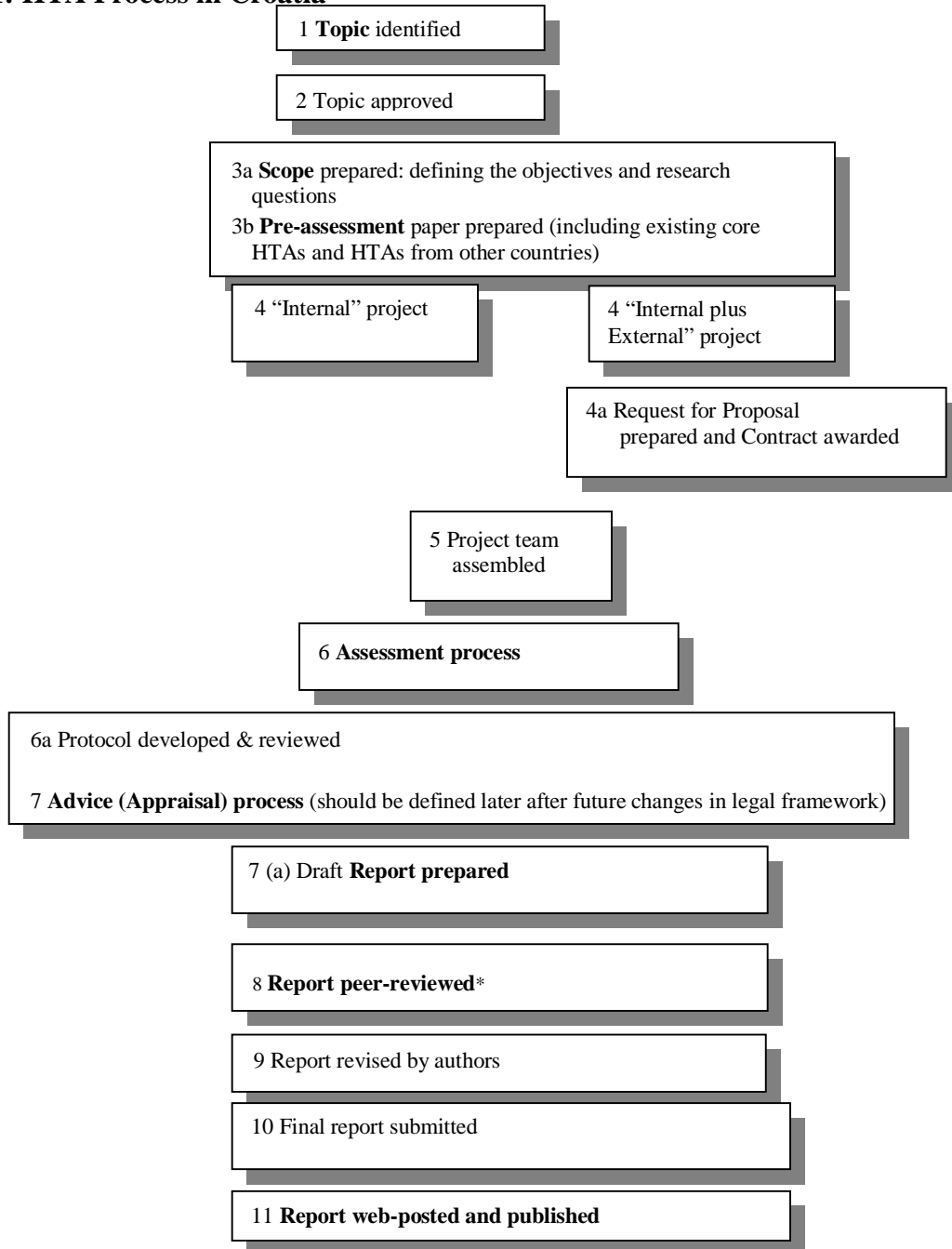
Throughout the life cycle of the report, it will be necessary to update each HTA Report every 2 years or earlier if there is significant new evidence that is likely to change the recommendations.



## II HTA process

HTA process in Croatia is presented briefly in Figure 1.

**Figure 1: HTA Process in Croatia**



## **1 Topics suggestion and selection process**

Topics suggested for assessment may come from various sources: Croatian Ministry of Health and Social Welfare, Croatian Institute for Health Insurance, private health insurance companies, industry, health professionals societies, clinical and public health professionals, patients associations, hospitals directors and policy teams, as well as Agency staff. Proposal will be submitted on the Agency HTA Topic Proposal Form, which can be found on Agency web site.

Agency HTA staff review each of the suggestions received to ensure they are appropriate and to check whether they are already included in its work. The suggestions are then filtered according to selection criteria and checklist:

- burden of disease (population affected, morbidity, mortality)
- resource impact (i.e. the cost impact on Croatian Institute for Health Insurance or the public sector)
- policy importance (i.e. whether the topic falls within a government priority area)
- whether there is an inappropriate variation in practice across the country.

Topics are approved and prioritized by the HTA Pharmaceutical Advisory Committee, and Devices and Systems Advisory Committee. The prioritization of topics occurs quarterly.

## **2 Scope prepared**

The ‘scoping’ process examines the appropriateness of the proposed topic and defines in detail what the assessment will and will not examine. Scoping is an important step because it determines the nature and content of the evidence included in the assessment. The purpose of a scope is to provide an assessment framework. The scope defines the issues of interest (for example, population and comparators) as clearly as possible and sets the boundaries for the assessment process. Recognizing the importance of views of different stakeholders in scoping process, such as representatives from main Croatian HTA users (Croatian Ministry of Health and Social Welfare, Croatian Institute for Health Insurance, hospitals) as well as health professionals, patients/caregivers groups, and manufacturers of health technology, their potential consultants are consulted on the

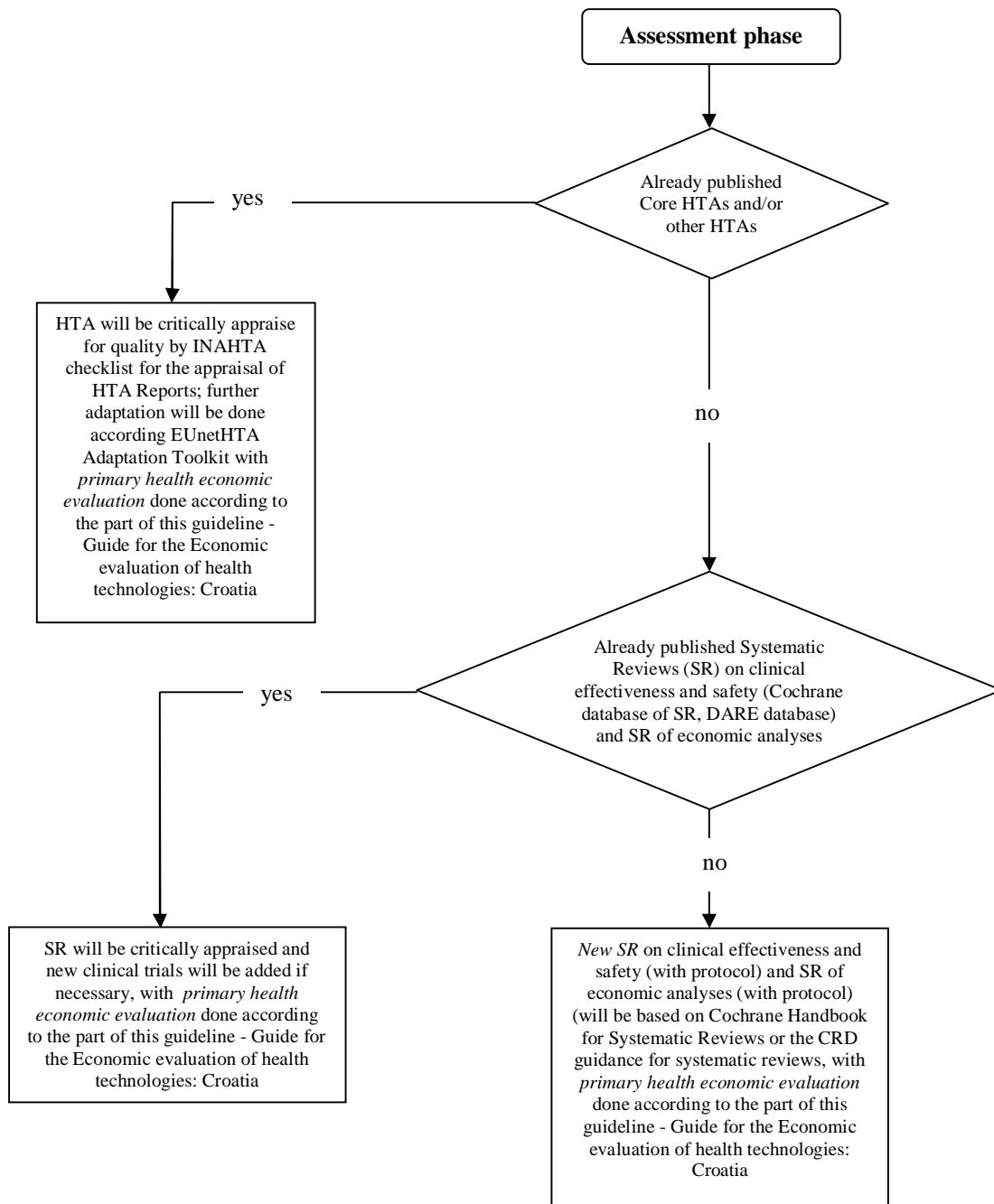
proposed topic and draft scope. This consultation process is designed to ensure that relevant issues have been considered and that the focus and boundaries of the assessment have been clearly defined in the final scope. It should be efficient and rapid as possible, conducted in open, transparent and consistent way, keeping in mind necessity of providing the decision-makers with useful, relevant, and timely information. After consultation process, a final scope will describe the boundaries of the assessment and the issues that will be investigated.

The final scope defines the issues of interest and the questions that should be addressed when considering the clinical, cost-effectiveness and other relevant domains of the technology as clearly as possible. The questions are fundamental to the assessment process and require an understanding of the context within which a technology is to be investigated, including currently available care and any alternative technologies for the specific indication. Objectives and research questions are defined for each approved topic. The first major step in the assessment process is to specify the questions of the review following the so-called **PICO structure** (**P**opulation/patients with the disease of interest; **I**ntervention(s), i.e. the technology under assessment; **C**omparison(s), which should serve as reference or gold standard and **O**utcomes which encompass the endpoints for assessing effectiveness and safety. Key questions based on PICO will drive the evaluation in the domain of clinical effectiveness, and the same often applies to the domains of safety and economics. In some cases, however, a subpopulation may be of specific interest in a certain domain due to specific details of safety or efficacy/effectiveness.

### **3 Assessment process**

A “pre-assessment” of the existing evidence on each selected topic is prepared by HTA Department staff (including existing Core HTA and/or HTAs from other countries). Final decision about HTA process, **Assessment phase**, will be done according to the Algorithm presented in Figure 2.

**Figure 2. Algorithm for HTA process (Assessment phase)**



Each project (according to the above algorithm in Figure 2) is designated as ‘internal’, or ‘internal plus external’, depending upon the resources available.

If *part of HTA* is designated ”external”, national as well as international academic and scientific institutions, and HTA Agencies, units or organization from EUnetHTA will be

contacted for a contract of specific HTA project. For each external project, an internal liaison researcher is appointed.

A multidisciplinary project team is assembled, composed of several analysts important for different HTA domains an information specialist and a clinical expert (“the authors”). All authors must satisfy established Agency’s Code of Practice for declaring and dealing with conflicts of interest in HTA process and authorship criteria. Members of the HTA Pharmaceutical Advisory Committee and Devices and Systems Advisory Committee are part of the multidisciplinary team up to and including the Protocol phase, but not beyond this phase.

For each project a Protocol is prepared. If the project is assessing a drug or medical device, industry will be contacted for information; Agency provides guidance on the process for this contact and format for document submission. A protocol specifies the plan or set of steps the authors will follow to complete the HTA report. The specific components will vary to some degree depending on the type of study undertaken. Common components include: background, objectives, proposed methods (including study selection criteria, data extraction and data analysis methods and forms) and roles of team members, detailed search strategy and timelines.

If already published Core HTA and/or HTAs from other countries exist, they will be critically appraised for quality by INAHTA checklist for the appraisal of HTA Reports and further adapted to Croatian setting according to EUnetHTA Adaptation Toolkit.

*Primary health economic evaluation* will be done according to the part of this guideline - Guide for the Economic evaluation of health technologies: Croatia,

If they do not exist, search for already published Systematic Reviews (SR) on clinical effectiveness and safety will be done in Cochrane database of SR or DARE database and SR of economic analyses in DARE database.

If such SRs exist, they will be critically appraised and new clinical trials will be added if necessary, along with *primary health economic evaluation* according to the appropriate section of this guideline - Guide for the Economic evaluation of health technologies: Croatia.

If such SRs do not exist, *new SR* on clinical effectiveness and safety (with protocol) and *new SR* of economic analyses (with protocol) will be done. Process of SR will be based on the new version of Cochrane Handbook for Systematic Reviews or on the CRD guidance for systematic reviews, with *primary health economic evaluation* done according to the section of this guideline - Guide for the Economic evaluation of health technologies: Croatia.

Recognizing the importance of patient involvement (patients perspective) for the entire HTA process, the Agency will invite patient representatives from patient organization or caregivers groups (those with direct personal experience of the condition and/or technology) to submit a short written view on the condition and technology and the way it should be used in Croatia, using a standard template (Patient/caregiver organization statement template; available on the Agency web site). Patients' representatives should be asked also to declare any possible conflict of interest with manufacturers of medical technologies. Patients' views will be published as attachment of the each Assessment Report.

#### **4 Advice (Appraisal) process**

The appraisal process (a consideration of the assessment report within the context of additional information supplied by consultants, commentators, clinical specialist, and patients experts (as active involvement of different Stakeholders), by the Appraisal Committee, for providing recommendation to decision-makers for their final decision), will be defined in the next versions of this Guideline, after future necessary changes in HTA legal framework (should be defined whether the Advise (appraisal) process is set up in the agency or if it separates from it). Members of the HTA Pharmaceutical Advisory Committee, and Devices and Systems Advisory Committee, will be appointed by the Agency. In the beginning they will serve as part of the research team up to and including the protocol phase, but not beyond this phase. In the future, if the Appraisal process becomes the responsibility of the Agency, they will serve in the appraisal.

#### **5 HTA Report**

There will be several types of the HTA report: Full HTA report in English language and Summary of full English report for the larger international community, Summary of full English report translated to Croatian language, Short Advice to the Minister of Health and Social Welfare and Short Advice to the Croatian Institute for Health Insurance in Croatian language, Short Advice to Hospitals, Short Advice to health professionals and Short Advice to patients, written in layman language. The authors will prepare the first draft of the full HTA report. Full HTA report should have the following headings and domains: Title, Authors, Conflict of interest statement, Executive Summary, Introduction

with scope, Current use of the technology (implementation level), Description and technical characteristics of technology and the comparator, Clinical systematic review of Effectiveness (adding Accuracy for diagnostic and screening techniques) and Safety, Economic part with systematic review of economic studies and primary economic evaluation, Ethical aspects, Organizational aspects, Social aspects, Legal aspects, Discussion section with summary of results, study limitations, generalizability of findings, knowledge gaps, and Conclusion, References and Appendices (as literature search strategy, large tables and figures....). The draft is reviewed internally, revised and then circulated to external, international reviewers who are experts in the subject area (including clinicians, methodologist, and economist). The authors will address the reviewers' comments. The final report will then be prepared, submitted and will receive a final review by research and communications staff. All types of reports (Full HTA report on English language and Summary of full English report for the larger international community, Summary of full English report translated to Croatian language, Short Advice to the Minister of Health and Social Welfare, and Short Advice to the Croatian Institute for Health Insurance in Croatian language, Short Advice to Hospitals, Short Advice to health professionals, and Short Advice to patients written in layman language) will be published on Agency's website and subsequently in print. All HTA Reports will get unique ID number and become a part of Agency Database on HTA.

## **6 Guide for the Economic evaluation of health technologies: Croatia**

### **The concept of the reference case**

The Agency has to make recommendations across different technologies and disease areas. It is, therefore, crucial that clinical and cost-effectiveness analyses undertaken to inform decision makers adopt a consistent approach. To allow this, the Agency has defined a 'Reference case' that specifies the methods considered by the Agency to be the most appropriate for the assessment process and recommendation for decision makers (Box 1).

## Box 1. Summary of the Reference case

<b>Element of HTA</b>	<b>Reference case</b>
Defining the decision problem	The scope developed by the Agency
Comparator	Therapies routinely used in the Croatian health system, including technologies regarded as current best practice
Perspective on costs	Croatian Institute for Health Insurance (Croatian Institute for Health Insurance as public payer) (societal perspective, including all cost and benefits outside the health care system, may be presented in addition, if considered relevant for some topics)
Perspective on outcomes	All health effects on individuals. If relevant, health effects in informal caregivers and/or family members can be reported separately
Type of economic evaluation	Cost-effectiveness analysis (CEA) or Cost-utility analysis, (CUA), depending on the particularities of the technology being assessed
Time horizon	Sufficiently long to reflect all important differences in costs or outcomes between the technologies being compared
Synthesis of evidence of outcomes	Based on a systematic review with/or without Meta Analysis (Head-to-Head RCTs preferred, indirect comparisons and observational studies may be accepted)
Measure of costs	Direct cost relevant to Croatian Institute for Health Insurance (where measurable and relevant, indirect costs and cost falling outside of Croatian Institute for Health Insurance should be reported separately)
Measure of health effects	Natural units (CEA) or QALYs (CUA)
Measurement of QALY gains	Reported directly by patients and/or informal caregivers
Source of preference data for valuation of QALYs	Representative sample of the public
Discount rate	An annual rate of 5% on both costs and health effects (in sensitivity analyses between 3% and 10%)
Equity weighting	None (an additional QALY has the same weight regardless of the other characteristics of the individuals receiving the health benefit)
Sensitivity analysis, Modelling, Subgroup analysis	Yes



Submissions from the Industry to the Agency, or part of HTA designated externally or performed internally, should include an analysis of results generated using these reference-case methods. This does not preclude additional analyses being presented when one or more aspects of methods differ from the reference case. However, these must be justified and clearly distinguished from the reference case. For example, analyses from a societal perspective (including all cost and benefits outside the health care system) may be presented in addition to reference case ones, if considered relevant for some topics.

There may be important barriers to applying reference-case methods. In these cases, the reasons for a failure to meet the reference case should be clearly specified and justified, and the likely implications should, as far as possible, be quantified. (The future Appraisal Committee will then make a judgment regarding the weight it attaches to the results of such a non-reference-case analysis).

### **Defining the decision problem**

Estimating clinical and cost effectiveness should begin with a clear statement of the decision problem. This will require a definition and justification of the technologies being compared and the relevant patient group(s) to be treated. These characteristics should be consistent with the Agency's scope for the HTA assessment.

The main technology of interest, its expected place in the pathway of care, the comparator(s) and the relevant patient group(s) will be defined in the scope developed by the Agency.

### **Comparator**

In the analysis, the costs and outcomes of therapies routinely used in the Croatian health care system, including technologies regarded as current best practice should be compared with the costs and outcomes of new technology. In addition, no treatment may be used as a comparator if it is the most commonly used practice.

### **Perspective**

#### *Perspective on costs*

The perspective adopted on direct costs should be that of the Croatian Institute for Health Insurance (Croatian Institute for Health Insurance as public payer, because the

appropriate objective of the Agency's technology assessment programme is to offer recommendation that represents an efficient use of available public payer resources). Direct costs are: drugs (directs costs of drugs and cost of drugs used to treat side-effects); medical services including procedures; hospital services; diagnostic and investigational services; and any other direct medical costs.

The resources should be valued using the prices relevant to the Croatian Institute for Health Insurance. Evidence should be presented to demonstrate that resource use and cost data have been identified systematically.

Technologies for which a substantial proportion of the costs (or cost savings) are expected to be incurred outside of the Croatian Institute for Health Insurance, or which are associated with significant non-resource effects other than health, should be identified during the scoping stage of an HTA process. In these exceptional circumstances, information on costs to other government bodies should be reported separately from the reference-case analysis.

#### *Perspective on outcomes*

For the reference case, the perspective on outcomes should be all direct health effects on patients. If relevant, also the health effects on other individuals (principally caregivers) should be included in the evaluation as well. These effects should be included separately from the analysis (i.e. descriptively) unless high-quality, reliable data on health effects in informal caregivers exist. The intention to include such data will normally be agreed with the Agency before finalization of the remit.

#### **Type of economic evaluation**

Cost-effectiveness (CEA) and cost-utility analysis (CUA) are the preferred form of economic evaluations. The decision to undertake either the CUA or the CEA should depend on the particularities of the health technology being assessed and on the availability of the data.

For the reference case, CEA should be applied and all direct health effects should be expressed in terms of natural units, such as: prevention of death, reduced incidence of complications, reduced side-effects, etc.

If the data is available, CUA should be performed instead of CEA (i.e. the outcome should be expressed in terms of Quality-adjusted life years or QALYs). The measurement of changes in QALYs should be reported directly from patients (or informal caregivers) and the value of changes in patients' QALYs (that is, utilities) should be based on public preferences using a choice-based method applied in a representative sample of the Croatian population.

The EQ-5D is the preferred measure of health-related quality of life in adults. The methods to elicit EQ-5D utility values should be fully described. When EQ-5D data are not available or are inappropriate for the condition or effects of treatment, the valuation methods should be fully described and be comparable to those used for the EQ-5D. Data collected using condition-specific, preference-based measures may be presented in separate analyses. The use of utility estimates from published literature must be supported by evidence that demonstrates that they have been systematically identified and selected. If CUA is applied, however, the information on life-years gained (saved) should also be presented.

Final outcome of the CEA and CEU should be the Incremental cost-effectiveness ratio (ICER).

### **Time horizon**

The time horizon for estimating clinical and cost-effectiveness should be sufficiently long to reflect all important differences in costs or outcomes between the technologies being compared.

### **Synthesizing evidence on outcomes**

The objective of the analysis of clinical effectiveness is the production of an unbiased estimate of the mean clinical effectiveness of the technologies being compared. The analysis of clinical effectiveness should be based on data from all relevant studies of the best available quality and should consider the range of typical patients, normal clinical circumstances, clinically relevant outcomes, comparison with relevant comparators and measures of both relative and absolute effectiveness with appropriate measures of uncertainty.

Synthesis of evidence on outcomes should be based on a Systematic review with or without Meta Analysis of RCTs. Head-to-Head RCTs are preferred, but indirect comparisons and observational studies may be accepted as well.

### **Indirect and mixed treatment comparisons**

If available, data from head-to-head RCTs should be presented in the reference-case analysis. When head-to-head RCTs exist, evidence from mixed treatment comparison analyses may be presented if it is considered to add information that is not available from the head-to-head comparison. This mixed treatment comparison must be fully described and presented as an addition to the reference-case analysis (a 'mixed treatment comparison' includes trials that compare the interventions head-to-head and indirectly).

When multiple technologies are being assessed that have not been compared within a single RCT, data from a series of pairwise head-to-head RCTs should be presented. Consideration should also be given to presenting a combined analysis using a mixed treatment comparison framework if it is considered to add information that is not available from the head-to-head comparison.

If data from head-to-head RCTs are not available, indirect treatment comparison methods should be used (an 'indirect comparison' is a synthesis of data from a network of trials). The principles of good practice for standard meta-analyses should also be followed in mixed and indirect treatment comparisons.

### **Discounting**

Cost-effectiveness results should reflect the present value of the stream of costs and benefits accruing over the time horizon of the analysis. For the reference case, an annual discount rate of 5% should be used for both costs and benefits, based on calculated mean of base rate for four quarters within respective year, over the last three year (reflecting the Croatian trend in Base rate and Discount rate over the last three years) according to Table 1 Base (reference) rate and Discount rate in the Republic of Croatia, from January 1, 2008 until January 1, 2011, Croatian Competition Agency, <http://www.aztn.hr/article/54/referentna-kamatna-stopa>, assessed on January 28 2011. When results are potentially sensitive to the discount rate used, consideration should be given to sensitivity analyses that use differential rates for costs and outcomes and/or that vary the

rate between 3% and 10% (reflecting the above mentioned Croatian trend in Base rate and Discount rate over the last three years).

### **Reflecting equity considerations in cost-effectiveness analysis**

In the reference case, an additional QALY should receive the same weight regardless of any other characteristics of the people receiving the health benefit. The estimation of QALYs, as defined in the reference case, implies a particular position regarding the comparison of health gained between individuals. Therefore, an additional QALY is of equal value regardless of other characteristics of the individuals, such as their socio-demographic details or their pre- or post-treatment level of health.

### **Modeling methods**

The models used to synthesize available evidence to generate estimates of clinical and cost-effectiveness for the Agency's needs should follow accepted guidelines. Full documentation and justification of structural assumptions and data inputs should be provided. When there are alternative plausible assumptions and inputs, sensitivity analyses of their effects on model outputs should be undertaken.

### **Characterization of potential bias and uncertainty**

It is important to identify potential selection bias in the inputs to the model and for the model to quantify the decision uncertainty associated with a technology (that is, the probability that a different decision would be reached if the true cost effectiveness of each technology could be ascertained before making the decision).

### **Dealing with uncertainty around the selection of data sources in cost-effectiveness analysis**

The uncertainty around the appropriate selection of data sources should be dealt with through sensitivity analysis. This will include uncertainty about the choice of sources for parameter values (both costs and effects). Such sources of uncertainty should be explored through sensitivity analyses, preferably using probabilistic methods of analysis.

Probabilistic sensitivity analysis is preferred for translating the imprecision in all input variables into a measure of decision uncertainty in the cost effectiveness of the options being compared. Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

### **Analysis of data for patient subgroups**

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. This should be explored as part of the reference-case analysis by the provision of estimates of clinical and cost effectiveness separately for each *relevant* subgroup of patients. The characteristics of patients in the subgroup should be clearly defined and should preferably be identified on the basis of an a priori expectation of differential clinical or cost effectiveness due to known, biologically plausible mechanisms, social characteristics or other clearly justified factors. When possible, potentially relevant subgroups will be identified at the scoping stage with consideration being given to the rationale for the expectation of a subgroup effect. However, this does not preclude the identification of subgroups later in the process (in particular, during the deliberations of the future Appraisal Committee).

### **Presentation of data and results**

#### **Presenting data**

All parameters used to estimate clinical and cost-effectiveness should be presented clearly in tabular form and include details of data sources. For continuous variables, mean values should be presented and used in the analyses. For all variables, measures of precision should be detailed. For probabilistic analyses, the distributions used to characterize the uncertainty in input parameters should be documented and justified. As much detail as possible on the data used in the analysis should be provided.

#### **Presenting expected cost-effectiveness results**

The expected value of each component of cost and expected total costs should be presented; expected QALYs for each option compared in the analysis should also be

detailed in terms of their main contributing components. Incremental cost-effectiveness ratio, ICER, should be calculated as appropriate.

### **The incremental cost-effectiveness ratio (ICER)**

Due the fact that Croatia still has not threshold value for the incremental cost-effectiveness ratio (ICER), defining it as the maximum societal willingness to pay for a quality-adjusted life year (QALY) or for life-year gained (LYG), as well as different recommendation from World Bank and WHO, the Agency will encourage discussion on this topic at national level with all stakeholders. Agency also recognizes that upper limit should not be fixed, and will depend also on other factors such as ethics and equity. Final recommendation for each technology will be based on all factors and domains of the HTA.

## **APPENDIX I: Bibliography of recommended HTA Guidelines and methodology references**

### **HTA Guidelines**

1. NHS National Institute for Health and Clinical Excellence. Guide to the methods of technology appraisal, 2008.
2. NHS National Institute for Health and Clinical Excellence. Guide to the single technology appraisal process, 2009.
3. NHS National Institute for Health and Clinical Excellence. Guide to the multiple technology appraisal process, 2009.
4. The Canadian Agency for Drugs and Technologies in Health (CADTH). Guidelines for Authors of CADTH Health Technology Assessment Reports, 2003.
5. Cleemput I, Van Den Bruel A, Kohn L, Vlayen J, Vinck I, Thiry N, et al. Search for Evidence & Critical Appraisal: Health Technology Assessment (HTA). Brussels: Belgian Health Care Knowledge Centre (KCE); 2007. KCE Process notes (D2007/10.273/40)
6. Kristensen FB, Sigmund H (ed.) Health Technology Assessment Handbook. Copenhagen: Danish Centre for Health Technology Assessment, National Board of Health, 2007, [http://www.sst.dk/publ/Publ2008/MTV/Metode/HTA\\_Handbook\\_net\\_final.pdf](http://www.sst.dk/publ/Publ2008/MTV/Metode/HTA_Handbook_net_final.pdf)
7. EUnetHTA documents: HTA Core Model for Medical and Surgical Interventions, and HTA Core Model for Diagnostic Technologies, <https://fio.stakes.fi/htacore/handbook.html>
8. EUnetHTA Adaptation Toolkit, [http://www.eunetha.net/upload/WP5/EUnetHTA\\_HTA\\_Adaptation\\_Toolkit\\_October08.pdf](http://www.eunetha.net/upload/WP5/EUnetHTA_HTA_Adaptation_Toolkit_October08.pdf)

### **Methodology references**

#### **Systematic Reviews and Meta-analyses of Clinical Effectiveness Studies**

1. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2 [updated September 2009]. The Cochrane Collaboration, 2009. Available from [www.cochrane-handbook.org](http://www.cochrane-handbook.org).
2. *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy*, Available from <http://srdta.cochrane.org/handbook-dta-reviews>
3. Egger M, Smith GD, Altman DG. Systematic reviews in health care: meta-analysis in context. 2<sup>nd</sup> ed. London: BMJ Publishing; 2001.



4. Khan KS, ter Riet G, Glanville J, Sowdena J, Keijnen J, editors. Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews. 2<sup>nd</sup> ed. York (UK): NHS Centre for Reviews and Dissemination, University of York; 2001. CRD report no. 4. Available: <http://www.york.ac.uk/inst/crd/report4.htm>
5. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009;6(7): e1000097.
6. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000;283:2008-12.
7. Moher D, Hopewell S, Schulz KF, Montori V, Gotzsche PC, Devereaux PJ, et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. BMJ. 2010;340:c869.
8. Bossuyt PM et al. The Standards for Reporting of Diagnostic Accuracy (STARD) Group. The STARD Statement for Reporting Studies of Diagnostic Accuracy: Explanation and Elaboration. Croat Med J. 2003;44:639-50.
9. Von Elm et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: Guidelines for Reporting Observational Studies. Ann Intern Med. 2007;147:573-77.
10. Vandembroucke JP et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): Explanation and Elaboration. Ann Intern Med. 2007;147:W-163-W-194. <http://www.equator-network.org/>, <http://www.consort-statement.org/>
11. INAHTA checklist for the appraisal of HTA reports: <http://www.dimdi.de/static/de/hta/methoden/sammlung/inahtachecklist.pdf>

### **The Economic evaluation references**

1. Canadian Agency for Drugs and Technologies in Health. Guidelines for the economic evaluation of health technologies: Canada [Internet]. 3rd ed. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006. Available from: [http://www.cadth.ca/media/pdf/186\\_EconomicGuidelines\\_e.pdf](http://www.cadth.ca/media/pdf/186_EconomicGuidelines_e.pdf)
2. Mittmann N, Evans WK, Rocchi A, Longo CJ, Au H.-J, Husereau D, et al. Addendum to CADTH's Guidelines for the Economic Evaluation of Health Technologies: Specific Guidance for Oncology Products. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.

3. Drummond MF, Sculpher MK, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. London: Oxford University Press; 2009.
4. Wells GA, Sultan SA, Chen L, Khan M, Coyle D. *Indirect Evidence: Indirect Treatment Comparisons in Meta-Analysis* [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009. (Technology report). Available from: <http://www.cadth.ca/index.php/en/hta/reportspublications/search/publication/884>
5. Consensus conference on economic modelling in health technology assessment; 1999 Apr 22-23; Sheffield, England. *Pharmacoeconomics*. 2000;17(5):443-513.
6. Drummond MF, McGuire A. *Economic evaluation in health care: merging theory with practice*. Oxford: Oxford University Press; 2001.

## **Appendix II: A Code of Practice for declaring and dealing with conflicts of interest in HTA process**



### **Agency for Quality and Accreditation in Health Care**

Department for Development, Research and Health Technology Assessment

## **A Code of Practice for declaring and dealing with conflicts of interest in HTA process**

**Issue date: February 2011**

This Document presents a combination of the following published documents which are adapted to Croatian setting: A Code of Practice for Declaring and Dealing with Conflicts of Interest (NICE), Form for Disclosure of Potential Conflict of Interest (IQWiG), and Guidelines for Authors of CADTH Health Technology Assessment Reports, The Canadian Agency for Drugs and Technologies in Health (CADTH), 2003.

The document is available from the Agency's website, [www.aaz.hr](http://www.aaz.hr)

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# **I CONFLICT OF INTEREST GUIDELINES**

## **Purpose of the Guidelines**

These guidelines are intended to ensure that all persons involved in the process of producing HTA reports, as well as other HTA documents, disclose any real or perceived conflict of interest situations.

## **Scope**

Conflict of interest guidelines apply to all individuals working on HTA process (HTA Assessment, Committee Appraisal and HTA Reports, as well as other HTA documents (all staff, consultants, contractors, collaborators, committee members, ad hoc groups, authors and reviewers of Agency for Quality and Accreditation in Health Care, Department for Development, Research and Health Technology Assessment), whether financial compensation has been or will be provided by Agency for Quality and Accreditation in Health Care.

## **Responsibility**

It is the joint responsibility of the Agency Director and the Assistant Director for HTA to ensure that all relevant parties complete a conflict of interest statement for each HTA project undertaken. It is the responsibility of the Assistant Director for HTA to ensure that such statements are accurately reflected in the published report and are also recorded in the project files (except for the amount of compensation, which remains confidential).

## **Compliance**

All relevant parties must comply with these conflict of interest guidelines as they ensure the integrity and impartiality of Agency and allow stakeholders to have confidence in Agency's objectivity. This policy requires individuals to make a thorough disclosure of real, potential or perceived conflicts of interest, specific and/or non-specific, financial, family and non-financial. Such conflicts may preclude participation in a particular project, but will not necessarily restrict participation in other projects.

## Description of Type of Conflict of Interest

Conflicts of interest (current or within the past three years, mentioned below) (*Specific* - for product under current evaluation and *Non-specific* – for other product, unrelated to the matter under consideration) are considered to be:

<b>Type of Conflict of Interest</b>
<b>1 Personal financial <i>specific</i></b>
2 Personal financial <i>non-specific</i>
<b>3 Personal family <i>specific</i></b>
4 Personal family <i>non-specific</i>
<b>5 Non-personal financial <i>specific</i></b>
6 Non-personal financial <i>non-specific</i>
<b>7 Personal non-financial <i>specific</i></b>

**Personal financial interest (1 and 2):** a current or within the past three years personal payment from manufacturer or owner or industry or sector of products; any consultancy, directorship, position in or work for healthcare industry that attracts regular or occasional payments in cash or in kind; any free-paid work commissioned by a healthcare industry for which the individual is paid in cash or in kind; any shareholdings, or other beneficial interest, in shares of a healthcare industry that are either held by the individual or for which the individual has legal responsibility; expenses and hospitality provided by a healthcare industry company including that required for accommodation, meals and travel to attend meetings and conference; funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

No interests exist in the case of accrued pension rights from earlier employment in the healthcare industry.

**Personal family interest (3 and 4):** Same as personal financial interest but applicable to family members.

**Non-personal financial interest (5 and 6):** payments or other benefit that benefits a department or organization for which an individual has managerial responsibility, but which is not received personally; the holding of a fellowship endowed by the healthcare industry; any payment or other support by the health industry that does not convey any

financial or material benefit to an individual personally but might benefit him or her like a grant from a company for the running of a unit or department for which a member is responsible, a grant or fellowship or other payment to sponsor a post or member of staff in the unit for which a member is responsible; the commissioning of research or other work by or advice from, staff who work in a unit for which the member is responsible.

**Personal non-financial (7) interest in a topic under consideration might include, but is not limited to;** a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review; a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence; holding office in a professional organization or advocacy group with direct interest in the matter under consideration, other reputation risk in relation to an intervention under review.

## **II WHEN SHOULD INTERESTS BE DECLARED AND WHAT ACTION IS REQUIRED?**

It is inappropriate for the Chair and members of the Agency Board, the Chair of its HTA Advisory or Appraisal Committees and Working Group, the Agency Director, Assistant Director for HTA or other employees, or the employees of the national and international academic or scientific collaborating centers which take a part of assessment, to have **any current personal** interest. Nor should they accept *direct* expenses or hospitality from the healthcare industries, as reimbursement for the reasonable and proportional costs involved in travel, accommodation and associated subsistence, for attending conferences at which they have been asked to speak or otherwise play a formal role. Such expenditure should be determined in accordance with the Agency's and organizations' speaking engagements policy and through organizations common donation funds without specifying the purpose of such donation; established committees will decide on priorities and purposes for this donations amount).

Appendix A sets out for each group, when a declaration of interest should be made. Appendix B summarizes the action which should be taken, when interest are declared at Advisory or Appraisal committee meetings.



*- ON APPOINTMENT*

The chair, the other board members, and employees of the Agency must declare all categories of interests on appointment, and then annually. This also applies to the chairs and members of the Agency HTA Advisory or Appraisal committee, other bodies and the staff of the national and international academic or scientific collaborating centers which take part in assessment process.

All people mentioned above should divest themselves of their personal financial interests on appointment, or as soon as is practical thereafter, but no more than 3 months after.

The declaration of personal family interests by a member or employee will not bar his or her employment or appointment to the Board or other body. When this personal family interest may have a bearing on specific aspects of the work of the employee at the Agency or at the national and international academic or scientific collaborating centers which take part in assessment, then the employee should discuss this with line manager who will set up appropriate arrangements to ensure that the interest does not conflict with the employee's duties.

Any uncertainty about potential conflicts of members of any bodies on appointment should be resolved at the discretion of the relevant chair and recorded in the letter of appointment. Members with conflicts that could be regarded as prejudicing their contribution to the discussion should be excluded from the group or committee. It is recognized that individuals may have some interaction with the healthcare industry and, while this should be declared, it does not necessarily preclude membership of an advisory body.

*- AT HTA Advisory or APPRAISAL COMMITTEE and other HTA BODY MEETINGS*

Members and other individuals covered by this Code who are attending to take part in the meeting should declare relevant interests at each body meeting and at appeal panels and state into which of the following categories they believe the interest falls.

A person with personal financial specific or personal family specific interest shall take no part in the proceedings as they relate to the intervention or matter and will normally leave the meeting until this matter has been concluded.

A person with personal financial non-specific interest- may take part in the proceedings unless, exceptionally, the chairs rules otherwise.

A person with non-personal financial specific interest or personal family non-specific interest may take part in the proceedings unless personal knowledge of the intervention or matter either through own work, or through direct supervision of others peoples work. In either of these cases person should declare this interest and not take part in the proceedings except to answer questions.

A person with non-personal financial non-specific interest may take part in the proceedings unless, exceptionally, the chair rules otherwise.

For personal non-financial interest the chair of the body shall determine, on a case-by case basis, whether person should take part in the proceedings.

#### SPECIAL NOTES ON COMPETITOR INTERVENTIONS

If a member is aware that an intervention or matter under consideration is, or may become, a competitor of an intervention developed, manufactured, sold or supplied by a company in which the member has a current personal financial or personal family interest, such person should declare an interest in the company marketing the rival intervention. The member should seek the Chairman's guidance on whether to take part in the proceedings.

#### - *IN EVIDENCE PUBLICATIONS*

Where an individual covered by this Code is responsible *for authoring*, in whole or part, of an HTA Report or other HTA documents, such individual must declare any interests in accordance with this Code.

### **III RECORD OF INTEREST AND THEIR PUBLICATION**

A record is kept at the Agency of:

Names of individuals who have declared interest on appointment, as the interests first arise or through the annual declaration and the nature of the interest; Names of individuals who have declared interests at meetings giving dates, names of relevant

interventions and companies, details of the interest declared and whether the member took part in the proceedings.

Information about any interests declared under this Code will be made publicly available on the Agency's website, in the form of a statement of annual declarations, through the minutes of advisory bodies or in guidance publications (except amount of compensation).

### **Appendix A: When is it necessary to declare an interest?**

	<b>Declaration on appointment</b>	<b>Annual declaration</b>	<b>Declaration at HTA Advisory or Appraisal Committee meeting</b>	<b>Declaration in evidence publication</b>
Agency Board chair and members	Yes	Yes	Does not participate	Does not author evidence publications
Agency employees	Yes	Yes	Yes	Yes
Agency HTA Committee chair	Yes	Yes	Yes	Does not author evidence publications
Agency HTA Committee member	Yes (except ad hoc groups)	Yes (except ad hoc groups)	Yes	Yes
Academic and scientific employee which takes part in assessment	Yes	Yes	Yes	Yes
Evidence contractor	Discuss with Agency	Not relevant	Yes	Yes
Expert advisor	Not relevant	Not relevant	Yes	Yes

## Appendix B: Declaring interest at an Advisory body meeting

Type of interest	See Page	Action
1 Personal financial specific	2	Declare and withdraw
2 Personal financial non-specific	2	Declare and participate (unless, exceptionally, the chair of the Advisory body rules otherwise)
3 Personal family specific	2	Declare and withdraw
4 Personal family non-specific	2	Declare and participate (unless, exceptionally, the chair of the Advisory body rules otherwise)
5 Non-personal financial specific	2	Declare and participate, unless the individual has personal knowledge of the intervention or matter either through own work, or through direct supervision of others peoples work. In either of these cases person should declare this interest and not take part in the proceedings except to answer questions.
6 Non-personal financial non-specific	2	Declare and participate (unless, exceptionally, the chair of the Advisory body rules otherwise)
7 Personal non-financial specific	2	Declare – action is at discretion of the chair of the Advisory body

## Appendix C: Definition of terms

*Professional Organizations:* refers to the public health professional associations, bodies and societies, universities, or any other bodies with whom the Agency has a contractual relationship or with whom the Agency is considering entering a contractual relationship

*Advocacy Group:* organizations whose functions include speaking for and on behalf of individuals and groups with an interest in health or health-related matters of the kind on which Agency issues guidance

*Members:* all members of the committees and groups

*Employees:* full and part-time on contract employees of the Agency

*Family members:* a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible

*Expert advisor:* clinical, patient or other expert invited to attend and take part in an Agency HTA meeting

*Evidence contractor:* organizations that the Agency contracts, directly or indirectly, to supply part of evidence

**Appendix D:**

**Agency for Quality and Accreditation in Health Care**

Department for Development, Research and Health Technology Assessment

**Form for disclosure of potential conflict of interest in Health  
Technology Assessment (HTA) process**

HTA project name and number:

**CONFLICT OF INTEREST STATEMENT**

All individuals working in the whole or in part of HTA process; on HTA assessment and HTA reports, as well as other HTA documents, Advisory or Appraisal Committee (all Agency staff, consultants, contractors, collaborators, committee members, ad hoc groups, authors and reviewers of Agency for Quality and Accreditation in Health Care, Department for Development, Research and Health Technology Assessment) are required to declare an interest that might be a conflict, or be perceived as conflict of interest.

Please indicate whether you have current or have had, within the past three years, any of the following affiliations with companies that manufacture health technology (products) which are *Specific* (for product under current evaluation) and *Non-specific* (for other product, unrelated to the matter under consideration):

<b>Type of interest*</b>	<b>Yes</b>	<b>No</b>
<b>1 Personal financial <i>specific</i></b>		
<b>2 Personal financial <i>non-specific</i></b>		
<b>3 Personal family <i>specific</i></b>		
<b>4 Personal family <i>non-specific</i></b>		
<b>5 Non-personal financial <i>specific</i></b>		
<b>6 Non-personal financial <i>non-specific</i></b>		
<b>7 Personal non-financial <i>specific</i></b>		

**\*Description of Conflict of Interest type:**

Conflicts of interest (current or within the past three years, mentioned below), *Specific* - for product under current evaluation and/or *Non-specific* – for other products, unrelated to the matter under consideration, are considered to be:

**Personal financial interest (1 and 2):** a current or within the past three years, personal payment from manufacturer or owner or industry or sector of products; any consultancy, directorship, position in or work for healthcare industry that attracts regular or occasional payments in cash or in kind; any free-paid work commissioned by a healthcare industry for which the individual is paid in cash or in kind; any shareholdings, or other beneficial interest, in shares of a healthcare industry that are either held by the individual or for which the individual has legal responsibility; expenses and hospitality provided by a healthcare industry company including that required for accommodation, meals and travel to attend meetings and conference; funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

No interests exist in the case of accrued pension rights from earlier employment in the healthcare industry.

**Personal family interest (3 and 4):** Same as personal financial interest but apply on family members.

**Non-personal financial interest (5 and 6):** current or within the past three years, payments or other benefit that benefits a department or organization for which an individual has managerial responsibility, but which is not received personally; the holding of a fellowship endowed by the healthcare industry; any payment or other support by the health industry that does not convey any financial or material benefit to an individual personally but might benefit him or her like a grant from a company for the running of a unit or department for which a member is responsible, a grant or fellowship or other payment to sponsor a post or member of staff in the unit for which a member is responsible; the commissioning of research or other work by or advice from, staff who work in a unit for which the member is responsible.

**Personal non-financial (7) interest in a topic under consideration might include, but is not limited to;** a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review; a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence; holding office in a professional organization or advocacy group with direct interest in the matter under consideration, other reputation risk in relation to an intervention under review.

**If yes to any of the above, please describe below, including approximate amount of compensation (the amount of compensation will be confidential):**

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Date

---

Name and Signature

## **Appendix III: Authorship Statement**

### **Authorship**

Authorship of Agency HTA Reports, as well as other HTA documents, complies with the following guidelines derived from the *Uniform requirements for manuscripts submitted to biomedical journals*. These were developed by the International Committee of Medical Journal Editors and are available at <http://www.icmje.org/>.

1. Each author participates sufficiently in the work to take public responsibility for appropriate portions of the content. One or more authors are responsible for the integrity of the work as a whole, from inception to the published report.
2. All persons designated as authors meet the criteria listed below, and all those who qualify are listed.

An author:

- substantially contributes to the conception and design of the study, or acquisition of data, or analysis and interpretation of data; and
  - drafts the report or revises it critically for important intellectual content; and
  - approves the final version.
3. Each author provides a description of his/her contribution, which is included in the published report, through completion of the authorship form (see below).
  4. The order of authorship is a joint decision of the co-authors. Authors should be prepared to explain the order in which they are listed.

### **Acknowledgements**

All contributors who do not meet the criteria for authorship, such as those who provided technical help or writing assistance only are acknowledged. Their function or contribution is described, e.g. “served as clinical advisor”, “critically reviewed the protocol” or “extracted data”.

**Insert Name and Project ID No. here**

**AUTHORSHIP FORM**

**Each author must submit a completed form to Agency when he/she has approved the final HTA Report or other HTA documents. All three of the criteria listed below must have been met in order to have authorship credit.**

---

Did you make substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data?

Did you participate in drafting the report or revising it critically for important intellectual content?

Have you provided approval on the version of the report submitted to Agency for publication?

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**Description of Contribution:**

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**Approval of final report submitted to Agency for publication:**

\_\_\_\_\_  
Name and Degrees

\_\_\_\_\_  
Position

\_\_\_\_\_  
Affiliation

\_\_\_\_\_  
Date



## **APPENDIX IV: Selected data sources on Croatian population health, healthcare resource use and costs**

1. Croatian National Institute of Public Health, <http://www.hzjz.hr/epocetna.htm>
2. Republic of Croatia - Central Bureau of Statistics, [http://www.dzs.hr/default\\_e.htm](http://www.dzs.hr/default_e.htm)
3. Croatian Institute for Health Insurance, <http://www.hzzo-net.hr/index.php>
4. MEDTAP International, <http://www.medtap.com/>  
(MEDTAP products and services are available by purchase. Examples are the Unit Cost Database, which provides unit costs for health care resources in Ontario and for some European and North American health systems; it also has Health Related Quality of Life data)