

**FORMAT FOR  
FORMULARY SUBMISSIONS**

**VERSION  
2.0**

*A Format for Submission of Clinical and Economic Data  
in Support of Formulary Consideration  
by Health Care Systems in the United States*



## ACKNOWLEDGEMENTS

The Academy of Managed Care Pharmacy (AMCP) and the Foundation for Managed Care Pharmacy (FMCP) gratefully acknowledge the contributions of many individuals who have devoted much time, expertise and commitment in the preparation of this valuable pharmacy tool.

Version 1.0 of AMCP's *Format for Formulary Submissions*, published in October 2000 was the culmination of nearly three years of mostly voluntary collaboration between talented authors experienced in the challenges presented by the complex task of appropriate formulary decision making: Joseph A. Gricar, MS, Regional Outcomes Research Manager, Pharmacia Corporation; Paul Langley, PhD, 3M Pharmaceuticals; Bryan R. Luce, PhD, MBA, CEO & Senior Research Leader, MEDTAP International, Inc.; C. Alan Lyles, PhD, MPH, BS Pharm, Associate Professor, University of Baltimore; and Sean D. Sullivan, PhD, Professor & Director, Pharmaceutical Outcomes Research and Policy Program, University of Washington Department of Pharmacy.

The *Format* would not have come about without the pioneering work of Dwight S. "Pete" Fullerton, PhD, RPh, and the pharmacy services staff at Regence BlueShield; as well as Dell B. Mather, PharmD, RPh, Senior Director, Pharmacotherapy Assessment and Policy, Prime Therapeutics, Inc. Their efforts in improving the evidentiary requirements for rational drug selection in managed care organizations served as a practical basis for evaluating the items considered for inclusion in this document. These guidelines have benefited directly and indirectly from their efforts.

By the Spring of 2002, efforts to have the *Format* process adopted by health systems and the pharmaceutical industry had progressed to the point that most of the major pharmaceutical companies were preparing product dossiers based on the AMCP *Format* at the request of numerous national managed health care systems, pharmacy benefit management companies, the Department of Defense, and a few hospitals and state Medicaid agencies. At this time, FMCP looked to Dr. Sean Sullivan to lead efforts to revise the *Format* by consolidating and addressing the hundreds of comments received since the *Format's* publication from pharmacists and other health care professionals representing managed health care systems, academia, and the pharmaceutical industry. The Academy and Foundation are deeply indebted to Dr. Sullivan for his continuing passionate support for the *Format* and his tireless devotion to evidence-based decision-making.

In addition to drawing on the expertise of most of the authors of Version 1.0, Dr. Sullivan was well served by members of the *Format* Revision Committee who acted as an expert review panel. We are indebted for the sage advice and constructive comments given by: Kerri Chitwood-Dagner, PharmD, BS Pharm, National Pharmacy Director, Great-West Life; Joseph A. Gricar, MS, Regional Outcomes Research Manager, Pharmacia Corporation; Dell Mather, PharmD, BS Pharm, Senior Director, Pharmacotherapy Assessment and Policy, Prime Therapeutics, Inc.; Marsha Moore, MD, MBA, Senior Vice President, Medical Affairs, AdvancePCS; Pete Penna, PharmD, Partner, Formulary Resources, LLC; and Nancy E. Stalker, PharmD, Vice President of Pharmacy Services, BlueShield of California.

The Academy and the Foundation are deeply indebted to Pete Penna, Partner, Formulary Resources, LLC, for his diligent work as FMCP Program Director for the *Format* from May 2001 to April 2002. The broad acceptance and rapid adoption of the *Format* process by health care systems and pharmaceutical manufacturers is directly attributable to his many years of experience in pharmacy benefit management, his meticulous attention to detail, and his continuing commitment to evidence-based decision-making as a fundamental requirement for improving patient health outcomes.



## BACKGROUND

The Academy of Managed Care Pharmacy (AMCP) published the *Format for Formulary Submissions* in October 2000. The AMCP Leadership and its members were motivated to develop these Guidelines by a growing need to ensure that any increased utilization of medications, biopharmaceuticals and vaccine products was appropriate and that newer products would bring added clinical and economic value to covered populations. To satisfy this need, the Academy recognized that it had to provide its members with the means to (1) promote the concept of combining efficacy, safety, effectiveness, and economic evaluation for the formulary decision-making process, (2) provide a consistent and direct means for manufacturers to supply information directly to health systems in order to support use of their products, and (3) break down cost silos and emphasize that simple acquisition cost reduction IS NOT the best approach to controlling overall health care expenditures.

Since publication of the AMCP *Format*, The Foundation for Managed Care Pharmacy (FMCP) has spearheaded an initiative to market its usage. This effort has included presentations and forums at AMCP and other professional organization's national meetings and conferences, articles in newsletters, peer-reviewed and lay literature, and numerous seminars designed to train health system pharmacists and pharmaceutical industry personnel on the appropriate use of the *Format*. Consequently, the *Format* has garnered nationwide publicity and attracted considerable attention, both positive and negative. Nevertheless, adoption of the *Format* process by health systems and the pharmaceutical industry has exceeded AMCP's and FMCP's expectations. Over the past two years a growing grassroots network has developed among health systems stimulating adoption initially by managed health care systems and PBMs and, most recently, by hospitals, integrated health care systems, state Medicaid agencies, and the Department of Defense. As adoption of the *Format* has spread, manufacturers have begun to standardize the framework within which they present population-specific data.

The *Format's* process is designed to maintain a high standard of objectivity to achieve two important goals. First, it is intended to improve the timeliness, scope, quality and relevance of information available to a health system's evaluators and ultimately to its P&T Committees. **However, health systems should not expect that its use would lower their drug expenditures.** A distinguishing feature of the *Format* is its use as an Unsolicited Request from a health system to a manufacturer for all possible clinical and economic information necessary to assess the overall clinical utility and value that a product brings to a specific patient population and health care system. In response to this Unsolicited Request, manufacturers are asked to submit all possible published and unpublished studies and information regarding both FDA-approved indications and anticipated off-label uses of the product. Therefore, this request improves access to material that has been difficult to obtain in the past. It also enables manufacturers to submit such data within regulatory constraints mandated by the Food and Drug Administration (FDA). While no explicit FDA guidance regarding unsolicited requests exists, FDA officials have repeatedly stated their intention to issue such guidance in the future. In the meantime, FDA officials have very clearly stated their position that they have responsibility for (1) assuring that requests for off-label product information are truly unsolicited and unprompted, (2) assuring that the information provided is not false or misleading, and (3) assuring that the response is specific to the requestor.

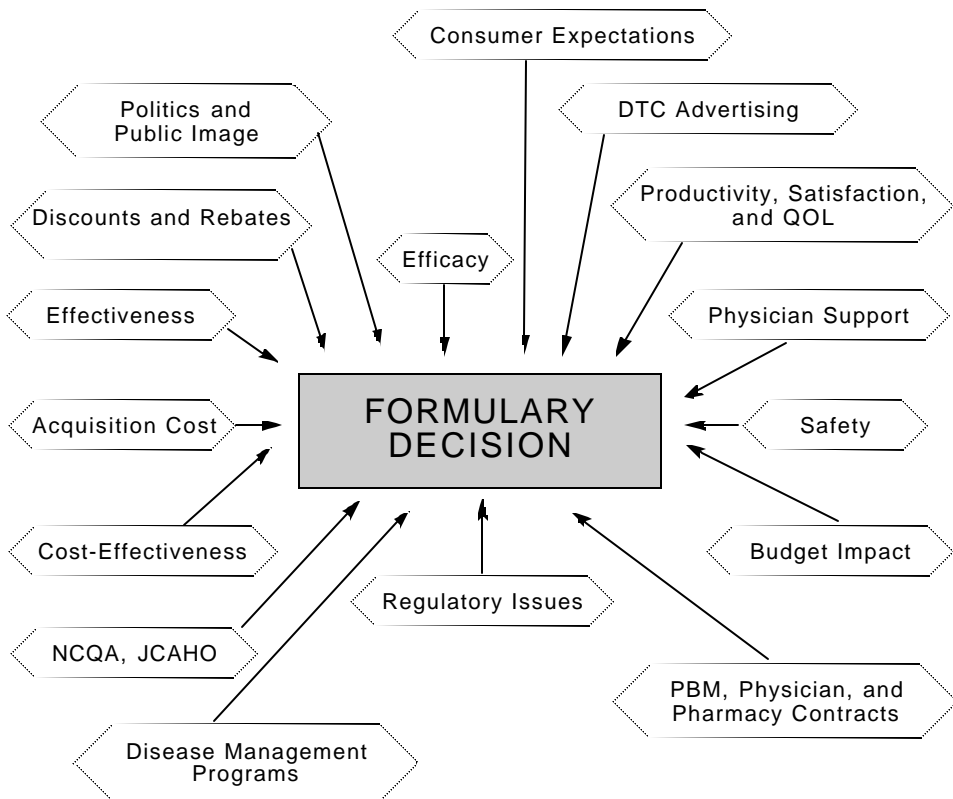
Health care professionals and health care systems worldwide are challenged daily to set priorities in an environment where demand for health care services outweighs the supply of resources allocated to finance it. In the absence of widely accepted models

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for legitimate and fair priority setting in health care, health care professionals must rely on the best available evidence to reach consensus about what constitutes a fair allocation of resources to meet competing health care needs. For example, formulary decision-making is frequently conducted under uncertain conditions due to the variability of available evidence on safety, effectiveness, and appropriateness of particular interventions. Gibson, et.al. state, “In the absence of consensus on guiding principles, the problem of priority setting becomes one of procedural justice — legitimate institutions using fair processes.”<sup>1</sup> By improving the timeliness, scope, quality and relevance of information available to P&T Committees, the *Format* strengthens the ability of health care systems to assess the impact of a particular product.

Figure 1



<sup>1</sup> Gibson JL, Martin DK, Singer PA. Priority setting for new technologies in medicine: A transdisciplinary study. *BMC Health Services Research*. 2002. 2:14. 18 July 2002.

## BACKGROUND

continued

Further, by assessing the health system impact of using a product, the data requested can improve the P&T Committee's ability to assess the effects of formulary alternatives on clinical outcomes and economic consequences for the entire health system. However, this information still must be weighed in the context of other values such as equity, social justice, the health of individuals as against communities, the "rule of rescue," and democratic decision making.<sup>1,2,3</sup> In addition, health care system priorities will be influenced by numerous other factors as represented in Figure 1.

Second, the *Format* will streamline the data acquisition and review process for health system staff pharmacists. By clearly specifying the standards of evidence implicit in the existing formulary process, the submission guidelines furnish pharmaceutical manufacturers with consistent direction concerning the nature and format of information that is expected. In addition, the standardized format allows clinical staff to formally evaluate the completeness of submissions received and to easily add the results of the health system's literature reviews and analysis. **Importantly, manufacturers should understand that submission of information in the format recommended does not guarantee approval of their product for formulary listing.** Discussion about, and subsequent receipt of, a dossier should be seen as a process to improve the quality and format of information provided, but not as a formula for approval.

Effective formulary deliberations require accurate, complete product dossiers best developed by manufacturers in partnership with health systems. Therefore, implementation of the *Format* calls for resource commitments by both health systems and manufacturers and a shared vision of the requirements to facilitate the collaboration necessary between the health system and manufacturers to support drug product evaluation.

Successful implementation of the *Format* process by a health system will include:

- a) Human, technical (IT) and financial resources to support the process within the plan including support of senior management and the P&T Committee;
- b) A commitment by all staff to make it work;
- c) Clear communication of *Format* requirements to pharmaceutical industry representatives;
- d) Health system pharmacy staff training in interpreting and integrating the data presented into the formulary process; and
- e) Accessibility to health system staff by industry representatives for presentations on data and economic models.

Part of a health system's use of the *Format* includes critical appraisal of the data supplied by manufacturers prior to its submission to the P&T Committee. In addition to a critical evaluation of the clinical information, the review should include an evaluation of the economic data by one trained in pharmacoeconomics. In order to evaluate the health economics information, health systems can use one of many published tools [see for example, guidelines for authors and peer reviewers reported in the *British Medical Journal*, Drummond and Jefferson, 1996 (see Appendix A)], which provide a checklist for health systems as a consistent measure of the quality and comprehensiveness of the report.

<sup>2</sup> Daniels N. Four unsolved rationing problems. Hastings Center Report. 1994, 24:27–29.

<sup>3</sup> Richardson J and McKie J. The rule of rescue. Working paper #112 (2000). Centre for Health Program Evaluation, Health Economics Unit, Monash University, Australia. <http://chpe.buseco.monash.edu.au/pubs/wp112.pdf>.

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Using the *Format*, the pharmaceutical industry will have the opportunity to justify the price of a new agent in terms of its overall value to the health system. In addition, industry scientists and consultants, using a reasonable scientific framework, will have the opportunity to provide additional information (e.g., adherence data, patient satisfaction, indirect and non-medical cost impacts) to demonstrate the broad value of their products when compared to usual treatments. Therefore, manufacturers have increased responsibility for providing relevant clinical data and economic impact information. The economic data called for must be broadly applicable to a health system's population and address the system-wide impact of formulary changes on both clinical outcomes and resource utilization and costs. The *Format* does not specify methods for economic evaluation. It is the submitter's responsibility to utilize appropriate techniques and data sources.

In response to similar requirements for reimbursement, pricing and formulary listing in Australia, Canada, the United Kingdom and other countries<sup>4,5,6</sup> pharmaceutical manufacturers are already submitting comprehensive reports on the effectiveness, safety and cost-impact of their products. The AMCP *Format's* requirements mirror these requests by requiring manufacturers to provide product dossiers that contain sufficient detail to give transparency to the analytical methods. However, the *Format* provides considerable flexibility. The formalized system suggested in AMCP's *Format* should be seen as a dynamic, rather than static, process. It is anticipated that increased standardization of information will lead to progressive improvement in the quality of submissions over time and provide health system pharmacists with data often unavailable in the past.

AMCP is not a standard setting organization. Therefore, the Academy has always viewed the *Format* as a template or guide, not a mandate or standard. As such, it does not claim to establish a standard of practice for managed care pharmacy. It is up to individual health care systems to decide how they will implement the *Format* and how they will operate their formulary review processes. For example, a health system may require dossiers for only new molecular entities. Another may require dossiers for all new products at launch and for existing products through their annual therapeutic class reviews. Others may choose to provide exceptions to the submission requirements for certain drug classes such as orphan drug products, chemotherapy agents and HIV/AIDS drugs. Ideally, products should only be considered for formulary review when the manufacturer can submit a complete dossier. Realistically, following an unsolicited request from a health system, manufacturers should make every attempt to submit a complete dossier. When evidence is missing, the manufacturer should provide the health system with a detailed explanation of what evidence is missing and a plan that addresses this deficiency within a specific time limit. If a dossier is not submitted following a health system's unsolicited request, the health system should reserve the right either to refuse to consider the product for formulary admission or to exercise other available options regarding the product's benefit status that are in keeping with its formulary and drug benefit management policies and procedures.

<sup>4</sup> Guidelines for the Pharmaceutical Industry on Preparation of Submissions to the Pharmaceutical Benefits Advisory Committee: including major submissions involving economic analyses. Australia. 1995 and 2000. <http://www.health.gov.au/pbs/pubs/pharmpac/gusubpac.htm> and <http://www.health.gov.au/pbs/pubs/pharmpac/interim/>.

<sup>5</sup> Guidelines for Economic Evaluation of Pharmaceuticals. Canada, 1997. [http://www.ccohta.ca/entry\\_e.html](http://www.ccohta.ca/entry_e.html).

<sup>6</sup> National Institute for Clinical Excellence. Great Britain. <http://www.nice.org.uk>.

## BACKGROUND

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The steady increase in the number of health systems adopting the *Format* have strengthened AMCP's and FMCP's conviction that this process represents the best opportunity for organizations to effectively implement a standardized and fair process for the evaluation of medications to determine how a specific product will impact overall health care delivery within their population. Therefore, the Academy and Foundation will continue to encourage the use of the *Format* as an essential tool to support product evaluation and selection with clinical outcomes as the most important consideration while avoiding the use of low acquisition cost and rebates as the *PRI-MARY* basis for selection. While cost considerations, under certain circumstances, may be relevant reasons for limits, in practice they tend to be highly controversial and contested. The recent backlash against managed care can be readily attributable to an American culture that is unwilling to accept limits. Writing in *Health Affairs* in 1998, Daniels and Sabin state "To change that culture requires a concerted effort at education, and education requires openness about the rationales for managed care plan's decisions."<sup>7</sup> By adhering to careful and thoughtful decision-making processes that provide the rationales for limits, health care systems will be able to show, over time, that "arguably fair decisions are being made and that those making them have established a procedure we should view as legitimate."<sup>3</sup> AMCP and FMCP believe that the *Format* is a tool that will help health systems establish a record of commitment to rational decision-making thus gaining the confidence of patients, clinicians, and members. The AMCP *Format for Formulary Submissions* is an essential tool to evaluate medications, but requires thoughtful consideration as it is used.

Since publication of the *Format*, AMCP and FMCP have continuously sought input from pharmaceutical manufacturers and health system pharmacists through various venues in order to improve and clarify the process. Version 2.0 is the first attempt to address users comments and concerns. Current and potential users of the *Format* will find that the Contents sections of the guidelines have not changed substantially. Our revision efforts in these sections were focused on providing additional clarity and making the document more user-friendly and understandable. We have attempted to address major areas of concern expressed by health system pharmacists and the pharmaceutical industry over the past two years in the following section — **Response to Comments**. We firmly believe that our efforts will result in more widespread acceptance and that grassroots efforts will lead to an ever-expanding network of adopters of the *Format* process. FMCP will continue its efforts to train health system pharmacists and pharmaceutical industry personnel on the appropriate use of the *Format*. The Foundation also assumes that further refinement of the *Format* will be necessary. To that end, FMCP staff will continue to solicit and catalog comments from users and potential users of the *Format*. In addition, FMCP is sponsoring formal research to critically evaluate the *Format* process to address ongoing concerns and to determine, among other things, its impact on health system's decision-making processes and on the pharmaceutical industry. Comments and ideas are always welcome and should be directed to Richard Fry, FMCP Director of Programs, (703) 683-8416, ext 345 or at rfry@fmcenet.org.

<sup>7</sup> Daniels N, Sabin JE. The ethics of accountability in managed care reform. *Health Affairs*. 1998; 17(5): 50–64.



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## OVERVIEW

### FOUNDATION OF A SOUND FORMULARY SYSTEM

Rational product adoption decisions employing clinical, economic, and humanistic data are built on the foundation of a sound formulary system. Pharmaceutical, biological and vaccine products should be subjected to a rigorous clinical review (and periodic re-review) based on evidence from the clinical literature. Evidence-based assessment of product efficacy, safety, effectiveness and cost-effectiveness provide the foundation for this review.

These precepts are affirmed by the National Committee for Quality Assurance (NCQA) managed care organization accreditation standard Procedures for Pharmaceutical Management and by the *Principles of a Sound Drug Formulary System*<sup>5</sup> developed and endorsed in August 2000 by AMCP and the Alliance of Community Health Plans, the American Medical Association, the American Society of Health-System Pharmacists, the Department of Veterans Affairs, Pharmacy Benefit Management Strategic Healthcare Group, the National Business Coalition on Health and the U.S. Pharmacopeia. (See Appendix B)

The goal of the [– –] formulary review process is to provide a quality pharmaceutical benefit determined through an evidence-based decision-making process taking into account the reality of constrained health care budgets. Where feasible, product comparisons should be made relative to existing competitor products as well as to placebo. For products with similar safety and efficacy profiles, decisions may be made primarily on net acquisition cost unless reasonable product value or other program efficiency arguments made by the manufacturer can be supported with pharmacoeconomic evidence. In other words, good economics does not make up for questionable clinical value.

### THE ROLE OF FORMULARY SUBMISSION GUIDELINES

Formulary submission guidelines support the informed selection of pharmaceuticals, biologicals and vaccines by:

- a) standardizing and communicating product and supporting program information requirements;
- b) projecting their impact on both the organization and its enrolled patient population; and
- c) making evidence and rationale supporting all choice(s) more clear and evaluable by [– –] decision makers.

These submission guidelines are intended to support an emphasis away from the product price/rebate approach often utilized for formulary decisions to one that emphasizes formulary decision-making based on evidence of clinical benefit, i.e. relative efficacy, safety and effectiveness and then total cost and health impact. Simply stated, manufacturers are asked to provide evidence of the clinical and economic value of their products for health system members — in terms of clinical benefits (efficacy and effectiveness), safety, health outcomes and overall economic impact. These guidelines emphasize that, while cost-benefit analysis and economic modeling are important elements in the value equation, they follow the principle clinical concerns of safety and efficacy. Importantly, manufacturers should understand that submission of information in the format recommended herein does not guarantee approval of their product for listing.

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continued

These guidelines are intended to offer a clear, shared vision of the requirements to facilitate the collaboration necessary between [– –] and manufacturers to support drug product evaluation. Recognizing that manufacturers may not have all the requested information for, especially, new products, this document describes the minimum information requirements necessary to support a comprehensive assessment of the proposed product.

***The Food and Drug Administration (FDA) and pharmaceutical manufacturers have generally regarded this Format as a detailed unsolicited request for information to support formulary evaluation by [...] clinical pharmacists. This request has enabled manufacturers to submit such data within existing regulatory constraints of the Food and Drug Administration.***

### GUIDELINES OVERVIEW

A complete formulary submission dossier for pharmaceutical, biological and vaccine products should include the following sections:

1. Disease and Product Information
2. Supporting Clinical and Economic Information
3. Cost-effectiveness and Budget Impact Model Report
4. Product Value and Overall Cost
5. Supporting Information: Reprints, Bibliography, Checklist, Electronic Media and Appendices

### CONTENT

These guidelines are not intended to restrict the content, presentation of data and the research methods of studies that comprise the dossier. Rather, they are intended to specify evidentiary requirements for product review. However in preparation of the evidence, the approach and methodology adopted by the manufacturer and the techniques employed should be consistent with the formulary evaluation objectives of [– –]. It is recommended that the manufacturer consult with [– –] representatives to determine appropriate sources for data and to agree on specific requirements and model assumptions. (See page 6 — Agenda for Pre-Submission Meeting)

### STANDARDS OF CARE AND DATA SOURCE

[...] recognizes that clinical development programs are designed, in large part, to meet regulatory requirements. When feasible, manufacturers are encouraged to consider the broader clinical and payer audience who require evidence on new drugs. For example, trial designs might be modified to reflect comparators of interest to [– –]. Furthermore, economic evaluations should be capable of reflecting the characteristics of the treatment environment of [– –]. Analyses based on clinical trials alone or data from other health systems or PBMs may be insufficient unless the manufacturer shows them to be directly applicable to [– –] membership. The manufacturer should focus on patterns of medical services provided directly by reasonable peer organizations. In some cases, there may be differences of opinion as to what constitutes appropriate standards of care. This should be resolved with [– –] prior to submission.

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## DISCLOSURE OF POTENTIAL REPORTING BIAS

To minimize the potential for bias in formulary submissions, manufacturers should follow generally-accepted rules of scientific conduct and reporting of clinical and economic evaluation data.<sup>2,3</sup> At a minimum, the following should be disclosed for economic evaluation studies, budget impact models and authors of the submission dossier:

1. Identify all investigators/authors and give the details of their affiliations.
2. All financial or contractual relations that might impact the independence of the investigators/authors.

## RECOMMENDED FORMULARY SUBMISSION PROCESS

*New Products*

The following steps are recommended for the submission of new drug products:

Step 1: Manufacturers should keep [– –] clinical pharmacy staff informed of the status of drugs in their pipeline. Both parties should identify specific contacts to ensure efficient communication.

Approximately 6 months prior to product launch, the [– –] pharmacy staff will issue a formal Unsolicited Request letter that contains a copy of the formulary submission requirements. The letter will be directed to the appropriate company employee who can engage in health professional-to-health professional communication, in compliance with FDA regulations on provision of label and off-label information.

Step 2: Following submission of the Unsolicited Request, [– –] pharmacy staff and manufacturer representatives may schedule an initial pre-submission meeting to establish a deadline for dossier submission based on the anticipated review date, and to discuss other pertinent issues such as commercial-in-confidence data, economic model assumptions, availability of spreadsheet models, etc. (*See page 6 — Agenda for Pre-Submission Meeting*).

Step 3: At least 2 months prior to the product review, the manufacturer will present one (1) paper copy and one (1) electronic copy of the submission dossier to [– –].

Step 4: The [– –] clinical staff assigned to the product will review the submission. Based on the initial review, the manufacturer may be asked to clarify certain points or submit additional information before a formulary monograph is prepared by [– –] staff for P&T review.

Step 5: The designated clinical pharmacists will prepare a detailed summary (monograph) for the P&T review. The summary presents an overview of all data, and the principal arguments for and against listing the product on formulary, and any conditions that may apply.

Step 6: As soon as possible, [– –] staff will inform the manufacturer of the P&T Committee's recommendation. Upon request, staff may provide the manufacturer with the rationale for a product's denial or restriction as well as guidance for reconsideration or appeal.

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**NOTE:** *Establishment of a formal appeals process is at the discretion of individual health care systems. Public entities, such as state Medicaid agencies, the Department of Defense or the Veterans Administration may be required by state or Federal law to have formal appeals processes in place to deal with denials related to formulary decisions.*

## AGENDA FOR PRE-SUBMISSION MEETING

This meeting(s) should take place at least 4-to-6 months before the actual date of anticipated product review to allow time for the manufacturer to gather the necessary data for [– –]. This meeting will also serve as a forum to discuss the consequences of missing information deemed necessary by [– –]. This agenda can serve as a discussion guide to ensure that [...] and the manufacturer address relevant topics. On-going communication between [...] should occur as deemed necessary.

The representatives for the manufacturer should provide a copy of, and be prepared to discuss, the following at the first meeting(s):

- a) List of intended indications
- b) Summary of studies to be included in the formulary submission.  
This will include:
  - ♦ Clinical trials (experimental and non-experimental)
  - ♦ Outcomes studies
  - ♦ Meta analysis
  - ♦ Retrospective studies
  - ♦ Economic and budget impact models
- c) Use of comparator products and their appropriateness
- d) A general description of how the cost and outcomes impact assessments will be developed. This should include:
  - ♦ List of data sources (studies, databases, etc.),
  - ♦ Discussion of incorporation of health system data,
  - ♦ Discussion of conversion of efficacy to effectiveness for both drug and comparators,
  - ♦ Approach to modeling the health care environment of [– –],
  - ♦ Discuss level of patient switching and impact on overall costs,
  - ♦ Assumptions and suggested approach for determining patient characteristics for switching.
- e) Summary of anticipated studies to be completed within 1–3 years
- f) A filled out submission checklist

## OVERVIEW

continued

## PERIODIC REVIEW OF THERAPEUTIC CLASSES AND REQUESTS FOR UPDATED DOSSIERS WHEN COMPETITOR PRODUCTS ARE BEING REVIEWED

Periodically, [– –] will undertake reviews of all drugs in each therapeutic class, including drugs currently listed and those that are non-formulary. Manufacturers may be asked to update their product dossiers with the most recent clinical data and economic modeling information. If required by [– –], this request will be made through issuance of a separate Unsolicited Request letter.

In addition, when a new competitor product is being reviewed, [– –] may ask manufacturers for an updated dossier for products with the same or very similar clinical profiles. In each case, manufacturers will be given as much notice as possible.

***NOTE:** Health care systems may choose to delete this section on annual review if their current P&T Committee procedures do not include a regular therapeutic class review.*

## ROLE AND RESPONSIBILITIES OF [– –]

[– –] clinical pharmacists welcome the opportunity to meet with manufacturers to review dossier submission requirements and to discuss data and analyses. As stated previously, [– –] should provide the manufacturer with timely information regarding product submission and evaluation such as:

- ♦ A dossier submission deadline;
- ♦ Anticipated date of initial product review or re-evaluation;
- ♦ General demographic information to assist in development of economic analyses, if feasible;
- ♦ Notification of additional information or data clarification requirements;
- ♦ The P&T Committee's recommendation.

By submitting this request [– –] recognizes that confidential information may be provided. [– –] recognizes the need to respect and honor commercial-in-confidence information and may be willing to sign necessary confidentiality agreements under agreed circumstances.<sup>16</sup>

As noted throughout this document, the success of the formulary submission process depends on an active collaboration between [– –] and the pharmaceutical industry.

## THE FORMULARY SUBMISSION DOSSIER

Manufacturers should complete their formulary submission dossiers using this *Format* to integrate the relevant published and unpublished data evaluating the efficacy, safety, economic impact, and other medical outcomes associated with the use of their product. Sections 1–4 should be completed and presented in the order listed. Compliance with this standardized reporting format allows for efficient review and facilitates the use of provided information by decision makers. Marked deviations from this format may delay the review process. While dossiers must provide sufficient detail to give transparency to the analytical methods used, the *Format* provides considerable flexibility. Where specific sections or data are unavailable or incomplete, the manufacturer should indicate and explain why they are missing and when they will be provided, if at all.

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Manufacturers should provide the following additional information:

- 1) A comprehensive list of references for all studies cited and for information sources from which estimates were drawn for use in the economic evaluation for section 2.4.
- 2) Identify the author(s) of the submission document. (*See Disclosure section above.*)
- 3) Identify the author(s) of primary economic evaluations conducted for section 2.3 of this document. (*See Disclosure section above.*)
- 4) Identify a contact person who can answer questions and provide additional information regarding the submission materials for [– –] reviewers.

# HEALTH SYSTEM GUIDELINES FOR MANUFACTUR- ERS

(Evidentiary Requirements for  
Formulary Submission Dossiers)

## SAMPLE UNSOLICITED REQUEST LETTER

Date

Name of Acct Manager/Medical Science Liaison

Name of Company

Address

Address

Dear...:

The [Organization name] has adopted the Academy of Managed Care Pharmacy's (AMCP) *Format for Formulary Submissions* detailing the process and evidentiary requirements for the provision of clinical and economic information to support drug formulary consideration. [Organization name] considers this document an unsolicited request for medical, economic and other scientific information (including any unpublished and/or off-label study data that are to be considered by our organization) and pharmacoeconomic modeling on all pharmaceutical products that we consider for formulary inclusion or as part of therapeutic class reviews. The specific details of the [Organization name] request have been sent to you previously and are available on the [Organization name] web site ([www.xxx.com](http://www.xxx.com)).

We consider this unsolicited request to represent the desired information to accompany a formulary submission. Manufacturers should submit a complete dossier well before they expect the product to be considered for formulary review. Our goal is to enable all of the [Organization name] Pharmacy & Therapeutics (P&T) Committees to make evidence-based decisions representing good value for money when selecting preferred treatment options. The AMCP *Format* describes a standardized template for pharmaceutical manufacturers to construct and submit a formulary dossier. The dossier is designed to make the product evaluation process in formulary development more complete, evidence-based and rational.

By submitting this request [– –] recognizes that confidential information may be provided. [– –] recognizes the need to respect and honor commercial-in-confidence information and may be willing to sign necessary confidentiality agreements under agreed circumstances.

Please consider this letter as an unsolicited request for information required by [Organization name] for your product Name of Product or Products here. If you require additional information, please call .....

Sincerely,

## HEALTH SYSTEM GUIDELINES FOR MANUFACTUR- ERS

(Evidentiary Requirements for  
Formulary Submission Dossiers)

### 1. PRODUCT INFORMATION

#### 1.1 PRODUCT DESCRIPTION [20 PAGES MAXIMUM]

Manufacturers are required to provide detailed information about their product. They should compare the new product with other agents commonly used to treat the condition, whether or not these products are currently on [– –] formulary. The product description consists of information that traditionally has been incorporated in a product monograph or formulary kit and includes the following:

- a) Generic, brand name and therapeutic class of the product,
- b) All dosage forms, including strengths and package sizes,
- c) The National Drug Code (NDC) for all formulations,
- d) A copy of the official product labeling/literature, and
- e) The AWP and WAC cost per unit size. (The [– –] contract price, if available, should be included as well.)
- f) AHFS or other Drug Classification
- g) FDA Approved and other Studied Indication(s): A detailed discussion of the approved Food and Drug Administration (FDA) indications and the date approval was granted (or is expected to be granted) must be included. Information on pending off-label indications and other non-labeled uses, if available, should be included.
- h) Pharmacology
- i) Pharmacokinetics/Pharmacodynamics
- j) Contraindications
- k) Warnings/Precautions
- l) Adverse Effects
- m) Interactions, with suggestions on how to avoid them
  - ♦ Drug/Drug
  - ♦ Drug/Food
  - ♦ Drug/Disease
- n) Dosing and Administration
- o) Access, e.g., restrictions on distribution, supply limitations, anticipated shortages
- p) Co-Prescribed / Concomitant Therapies, including dosages
- q) Comparison with the pharmacokinetic / pharmacologic profile of other agents in the therapeutic area. The material may include a discussion of comparator product(s) or services that the proposed product is expected to substitute for, or replace (including drug and non-drug interventions). This information should be presented in tabular form.

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## 1.2 PLACE OF THE PRODUCT IN THERAPY [LIMIT 1–3 PAGES]

The disease description should include the disease and characteristics of the patients who are treated for the condition. Present a brief summary of information from the literature for each topic. When information from studies is presented, the manufacturer should compile the results in detailed evidence tables.

Next, an attempt should be made to generalize these findings to the populations of [– –]. Discuss the implications of any differences that exist between the literature and typical practice patterns and patient populations. When more than one disease is addressed, complete the description for each separate condition.

Specific disease descriptive information requested: [Not more than 2–3 pages per disease]

- a) Epidemiology and relevant risk factors
- b) Pathophysiology
- c) Clinical presentation
- d) Approaches to treatment — principal options / practice patterns
- e) A description of alternative treatment options (both drug and non-drug)
- f) The place and anticipated uses of the proposed therapy in treatment (e.g., first line)
- g) The expected outcomes of therapy and
- h) Other key assumptions and their rationale.

[– –] and the manufacturer should determine the relevant treatment options for comparison during the initial pre-submission meeting.

## 2. SUPPORTING CLINICAL AND ECONOMIC INFORMATION

### 2.1 SUMMARIZING KEY CLINICAL AND ECONOMIC STUDIES

Submit the key clinical and economic studies that have been conducted, whether published or not, for clinical safety, efficacy, economic and health outcomes evaluations. Studies reported in this section should be summarized in a clear, concise format; presenting data from multiple studies in tabular form within a category is strongly encouraged. All of the following that apply should be included:

- a) Name of the clinical trial or study, location and study date;
- b) Trial design, randomization and blinding procedures;
  - ♦ Research question(s);
  - ♦ Study perspective;
- c) Washout, inclusion and exclusion criteria;

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- d) Sample characteristics (demographics, number studied, disease severity, co-morbidities);
  - ♦ Treated population (actual or assumed)
- e) Patient follow-up procedures (e.g., If an intention-to-treat design is used, were drop-outs followed and for what time period?);
  - ♦ Treatment period
- f) Treatment and dosage regimens;
  - ♦ Treatment framework
  - ♦ Resource utilization classification
  - ♦ Unit costs;
- g) Clinical outcome(s) measures;
  - ♦ Outcomes evaluated;
- h) Other outcome measures (e.g., quality of life);
  - ♦ Principal findings
- i) Statistical significance of outcomes and power calculations;
- j) Validation of outcomes instrument (if applicable);
- k) Compliance behavior;
- l) Generalizability of the population treated;
  - ♦ Relevance to enrolled populations of [– –].
- m) Publication citation(s)/references used.

### 2.2 PUBLISHED AND UNPUBLISHED CLINICAL STUDY RESULTS [2 PAGE MAXIMUM PER STUDY; PLEASE COMPLETE EVIDENCE TABLES IN THE [– –] FORMAT

Provide summaries addressing items a–m (*see 2.1 above*) for studies in each of the categories listed below (items a–d). The manufacturer should complete evidence tables that summarize the data. [– –] is particularly interested in head-to-head comparison clinical studies between the proposed product and the principal comparators. Summaries of trial results of key comparator products are desirable but not required. Discuss important study findings and comment on their implications for the patient populations represented by [– –]. Systematic reviews or meta-analyses may be referenced in item (e). In the appendix, include a reprint or unpublished manuscript of each study discussed or referenced:

- a) Pivotal safety and efficacy trials [Usually no more than one (1) page per study + evidence table]
- b) Prospective effectiveness (e.g., large simple) trials [usually no more than one (1) page per study + evidence table]
- c) Additional prospective studies examining other non-economic endpoints such as health status measures and quality of life. If the instruments utilized in these studies are supported by previous validation and reliability studies, also refer-

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ence these studies. [No more than one (1) page per study]

d) Retrospective studies [No more than one (1) page per study + evidence table]

e) Review articles and meta-analyses. Place particular emphasis on the inclusion and exclusion criteria and main outcome measure(s) for studies analyzed.

In addition, information from all known studies on the product should be summarized in a spreadsheet format (item f), noting which studies were presented previously (items a–d).

f) Evidence table spreadsheets (noted above) of all published and unpublished trials. A standard evidence table format, such as that contained in Appendix C, Template for P&T Monograph, should include the following data elements:

- ♦ Citation, if published
- ♦ Design
- ♦ Sample size
- ♦ Inclusion/exclusion criteria
- ♦ Endpoints
- ♦ Statistical significance
- ♦ Study dates
- ♦ Results
- ♦ Treatments

## 2.3 CLINICAL AND DISEASE MANAGEMENT INTERVENTION STRATEGIES

[3 PAGES MAXIMUM]

Identify and summarize any proposed ancillary disease or care management intervention strategies that are intended to accompany the product at launch.

## 2.4 OUTCOMES STUDIES AND ECONOMIC EVALUATION SUPPORTING DATA [2 PAGES MAXIMUM PER STUDY]

Concern has been expressed over the quality of some published economic evaluations.<sup>3,4,11</sup> Since the focus of this portion of the dossier is a comprehensive assessment of available evidence, the number of studies considered will not be restricted by imposing methodological standards. However, [– –] and its consultants will judge the merit of individual studies based on published standards for conducting and reporting these analyses.<sup>4,12</sup>

Provide summaries addressing items a–m (*see 2.1 starting on page 11*) for all studies in each of the categories listed below (items a–d). [– –] is particularly interested in head-to-head comparison studies between the proposed product and the principal comparators. Analyses that focus on actual outcomes rather than intermediate endpoints are preferred. Summaries of principal trial results of key comparator products when these data are referenced or used in economic models are extremely helpful, but not required. Discuss important study findings and comment on their implications for the patient populations of [– –]. In the appendix, include a reprint of each study discussed or referenced:

- a) Prospective cost-efficacy studies [No more than two (2) pages per study + evidence table]
- b) Prospective cost-effectiveness studies trials [No more than two (2) pages per study + evidence table]
- c) Cross-sectional or retrospective costing studies, treatment pattern studies or

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economic evaluations [No more than two (2) pages per study + evidence table]

- d) Review articles
- e) Spreadsheet of all published and unpublished economic evaluations utilizing the format specified in Section 2.2, Item (f), noting which studies were presented previously (items a–d).

### 3. MODELING REPORT [MAXIMUM 20 PAGES]

#### 3.1 MODEL OVERVIEW

Properly constructed economic and budget impact models can combine treatment effectiveness, the resources consumed (and costs) by each treatment process, and a measure of uncertainty in any estimates. The goal is to project the health and economic consequences of [– –] formulary changes. Models developed in this manner can:

- ♦ Aid decisions regarding the addition of a new product to the formulary,
- ♦ Help define a product’s specific role, and
- ♦ Assist in creating benchmarks against which the product’s future performance can be measured.

Specifically, these analyses should depict the following:

- a) Disease or condition, patient population, natural history, clinical course and outcomes.
- b) Primary treatment options and the treatment process for each option. Each process of treatment utilizing a specific product or other intervention follows a clinical pathway. If the [– –] employs a treatment guideline for this condition, this framework should be followed. Alternative clinical pathways presented by the manufacturer may also be considered.
- c) Patient population eligible for treatment.
- d) Product and other medical resources used when following clinical pathway (include treatments for complications related to treatment).
- e) Costs of product and other medical resources consumed within each clinical pathway.
- f) Outcomes of therapy for each clinical pathway, including expected proportion of treatment failures and mean or median time to failure, if known. These outcomes can be broadly and uniquely defined by the manufacturer and can be modeled from other data sources. The manufacturer should address the relevance of the selected outcomes measure and generate both baseline and projected outcome impact assessments.
- g) Incremental cost and outcomes analysis presented in either cost/consequences tables or as cost-effectiveness ratios.
- h) Time horizon for expected costs and outcomes. Suggested time horizons include 1-year, 5-year and over the course of the disease. The exact time horizon used

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will depend on the natural course of the disease. In some cases, multiple time horizons might be appropriate.

In addition, the manufacturer is requested to:

- i) Separate the volume of resources utilized and the unit costs for each resource.
- j) Perform sensitivity analyses on pivotal estimates and assumptions and display a one-way sensitivity analysis of all variables in a tornado diagram.
- k) Consult with [– –] staff in the early stages of model development to ensure the incorporation of appropriate comparator products and endpoints.
- l) Present the following information in tabular form: data and sources, assumptions, total resource utilization, total costs, total effectiveness, incremental costs, and incremental effectiveness. Measures of total and incremental effectiveness should incorporate natural units (e.g., clinically important events avoided) as well as quality-adjusted survival when possible.

The analysis should be based on scientifically appropriate clinical trial, epidemiological and economic data and should be capable of being modified by [– –] to better reflect practice patterns in their enrolled population. For the analysis and model to be realistic, it may be necessary to include data from [– –], e.g., demographic data. Data derived from expert panels are not generally acceptable, especially for key clinical and treatment pattern variables. But this approach may be understandable for other variables where estimates are not available through literature, databases, trials or other normal sources.

The model framework should consider recommendations published by the *Panel on Cost-Effectiveness in Health and Medicine* convened by the U.S. Public Health Service.<sup>8</sup> Although no standard model approach is proposed, good modeling practices should always be followed. We have found that models have certain desirable qualities. These are listed below and are in no way meant to proscribe model development or impede good scientific design. Rather, this list is to provide some guidance to the manufacturer as to those elements of an economic model that are desirable to [– –] evaluators.

### *Desirable Qualities of Economic Models for Inclusion in [– –] Submissions*

#### **Model Structure**

- ♦ A transparent disease progression model with an appropriate time horizon for a health system.
- ♦ Treatment pathways that are relevant to the formulary decision and correspond to nationally recognized or [– –] treatment guidelines. To help illuminate the proposed treatment pathways, the manufacturer is encouraged to provide decision trees.
- ♦ Usual clinical practice, including relevant comparators to [– –], is included in the model.
- ♦ Mathematics and calculations included in the model are accurate and available for inspection.
- ♦ Allowance for analysis of relevant sub-populations (age, gender, co-morbidities) where applicable.
- ♦ An interactive model that allows the health system to incorporate its own data

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(membership size, prevalence rates, cost estimates, etc.) or, if requested, use default data, such as national norms.

### *Data*

- ♦ Sources of data are clearly defined and from the most recent studies.
- ♦ Data have been interpreted and accurately incorporated into the model.
- ♦ Uncertainty is defined, especially for key variables.
- ♦ Linkages between intermediate and longer-term endpoints are valid and based on reasonable scientific evidence.
- ♦ Assumptions that drive the model are clearly identified.

### *Results/Output*

- ♦ Outcomes need to be relevant to the [– –] formulary decision.
- ♦ Incremental analyses of both health effects and costs.
- ♦ Results are verifiable and traceable back to the inputs.
- ♦ Uncertainty in model and data tested in a reasonable fashion and reported.
- ♦ A tornado diagram depicting the results of a comprehensive (on all variables) one-way sensitivity analysis.
- ♦ Results presented in such a fashion that facilitates incorporation into drug reviews and monographs.

The model's time frame is a critical element. For chronic illnesses, a one to three-year period should be adopted as well as a longer period, as appropriate for the clinical problem and its resolution. For this longer period, a final and disease appropriate health outcome determination is recommended, possibly including more patient-centered outcomes, such as Quality of Life Year Saved. For acute illness, shorter periods may be appropriate.

### 3.2 PARAMETER ESTIMATES FOR MODELS

Randomized, controlled efficacy studies are required for licensing and registration. These data comprise the foundation for FDA approval, labeled indications and marketing. [– –] recognizes that manufacturers must conduct these studies for the FDA. In addition, [– –] recognizes that the results observed in randomized trials are likely to represent optimal effects and are difficult to generalize to populations because of patient selection and the close oversight given subjects in clinical trials.

In general, the best quantitative estimates of clinical effectiveness are required, with uncertainty in the estimate(s) handled analytically via sensitivity analysis. Thus, where possible, feasible and scientifically plausible, scientists preparing the economic model are encouraged to attempt transformation of efficacy results into effectiveness parameters. This may involve inclusion of an adherence parameter into the model or may involve the creative use of retrospective data. Documentation and clear description of the methodology will be necessary in order for [– –] staff to evaluate the validity of this approach.

Translation of claims from an efficacy to an effectiveness context should be considered when:

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- a) The model's treatment period extends beyond that represented by the clinical trial;
- b) Outcomes supported by the trial are intermediate or surrogate in nature;
- c) Compliance, dosing, co-morbid conditions and the population of interest (e.g., children, elderly) are expected to differ from the efficacy trial data.

Poor adherence to therapy, especially for chronic conditions, can impact manufacturer claims that are based exclusively on carefully monitored clinical efficacy trials. All claims (promotional or otherwise) made for new products should state clearly the assumptions concerning patient adherence. It is suggested that manufacturers provide documentation of anticipated adherence patterns from populations similar to the treatment populations of [– –], if available. This may be more plausible for manufacturers who have launched products in other countries before the US introduction.

### 3.3 PERSPECTIVE, TIME HORIZON AND DISCOUNTING

The payer perspective is recommended for the primary analysis. We welcome a societal perspective analysis as a secondary evaluation. The analytic model should consider a time horizon that is appropriate to the disease being studied and reflect the decision-making and financial and budget constraints of [– –]. When appropriate, adjustment for the time preference should be incorporated and should follow US PHS Panel recommendations.<sup>8</sup>

### 3.4 ANALYSES

Analyses should follow accepted approaches for economic models. Transparency and clarity of presentation make for understandable modeling exercises. [– –] staff needs to be able to understand all steps in the modeling process, so researchers are encouraged to spend time thinking about clarity and transparency of results.

All assumptions must be presented and justification should be attempted.

A tornado diagram with a comprehensive (all variables) one-way sensitivity analysis is highly recommended. Base case and other appropriate sensitivity analyses also are recommended. Confidence interval determination, best/worse case scenario analyses, net-benefit and acceptability curve estimation are allowable as necessary and appropriate.

When a product is to be used in the treatment of more than one disease, its impact should be modeled for each approved indication, unless a reasonable case can be made for a single model. Because of the complexity involved in constructing a model that simultaneously addresses several indications, we recommend using a separate model for each condition.

### 3.5 PRESENTATION OF MODEL RESULTS

Results should be presented as follows:

- a) Disaggregated results (cost-consequence presentation style) should be presented before viewing incremental cost-effectiveness ratios. These data are more easily understood and interpretable by the [– –] formulary committees.
- b) Costs should be presented as total medical and pharmacy costs of introduction

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of the new product and then disaggregated into various resource components including drug costs. Estimates must include the cost of any additional resources associated with implementing the therapy (e.g., disease management).

- c) Health effects should be presented in disaggregated form before inclusion in a ratio.
- d) Sensitivity analyses are to be shown in tabular or graphical form (tornado diagram), with the base case results displayed alongside.
- e) Factors that drive the cost and cost-effectiveness results must be presented clearly (for example, tornado diagrams).

### 3.6 EXCEPTIONS

A pre-existing model developed for another health system or for another country may eliminate the need to develop a new model for this submission. A model based on national norms may also be acceptable provided it is submitted in such a manner (spreadsheet) that [...] can either use the default values or insert its own. To be acceptable, the existing model should follow the general framework described in this document and must be able to demonstrate the system-wide impact of introducing the product to [– –] formularies. It is the manufacturer’s responsibility to justify the adequacy of pre-existing models. Developing a model that can be adaptable and allow [...] to make changes in multiple elements will greatly enhance this process.

## 4. PRODUCT VALUE AND OVERALL COST [2 PAGE MAXIMUM]

This section of the submission requirements represents the principal opportunity for a manufacturer to communicate the value of its product to [– –]. The manufacturer should briefly summarize the information presented previously, state the expected per unit product cost, and estimate the total pharmacy expenditures of [– –] for the product. Based on this information, the manufacturer should articulate a value argument to justify these expected expenditures for this product in the context of its anticipated effects on the clinical and other outcomes and the economic consequences for [– –] and its clients and members. Through this process, product value is redefined as both parties move beyond cost containment to focus on optimizing drug utilization in an environment of limited resources.

## 5. SUPPORTING INFORMATION

### 5.1 REFERENCES CONTAINED IN DOSSIERS

Submissions should list and provide copies of all clinical and pharmacoeconomic references made in Sections 2 and 3 above.

### 5.2 ECONOMIC MODELS

Media: In addition to the written report, the manufacturer must provide a transparent, unlocked copy of the model without the graphical interface. It should be presented on a

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3.5” disk or CD-ROM as an Excel workbook, ASCII tab-delimited file or an alternative format that is agreed upon by [– –] or its consultants and the manufacturer. The model should be transparent, i.e., designed to allow staff or consultants to investigate the assumptions and calculations, and to perform independent sensitivity analyses by varying individual parameters. [...] **will retain this model for internal analyses and will not release it to any other party.** Manuscripts that support the development and reporting of the model are to be attached as appendices.

## 5.3 FORMULARY SUBMISSION CHECKLIST

A. SUBMISSION PROCESS		
A.1 Have you met with [– –] staff to review the submission process?	Yes	No
A.2 Have you agreed to the submission date with [– –]?	Yes	No
A.3 Have you requested estimates to identify baseline characteristics of the populations of the health systems represented by [– –]?	Yes	No
A.4 Have you included an explanation for any missing data? (Check yes if N/A)	Yes	No
A.5 Have you submitted a copy of the dossier in both paper and electronic form?	Yes	No

**A completed formulary submission checklist should accompany each submission.**

B. PRODUCT INFORMATION		
B.1 Has a product description been provided for the product?	Yes	No
B.2 Has a list of approved indications been given for the product?	Yes	No
B.3 Has the place of this product in therapy been given for each indication?	Yes	No
B.4 Have copies been provided of treatment guidelines for this product?	Yes	No
B.5 Have intermediate and final outcomes of therapy for this product been listed?	Yes	No
B.6 Have you listed any co-prescribed drugs for this product by indication?	Yes	No
B.7 Have you identified the comparator drugs for this product by indication?	Yes	No

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C. SUPPORTING CLINICAL INFORMATION		
C.1 Have you identified all relevant clinical and other studies for the product and its comparators?	Yes	No
C.2 Are copies of all summarized studies included in the submission package?	Yes	No
C.3 Have you provided an electronic spreadsheet summary of all studies identified using the [- -] format?	Yes	No
C.4 Have you included all relevant non-experimental studies for the product?	Yes	No
C.5 Have you provided an electronic spreadsheet summary of all non-experimental studies using the [- -] format?	Yes	No

**A brief explanation for all missing data should also be included.**

D. SUPPORTING ECONOMIC INFORMATION		
D.1 Have you identified all relevant pharmacoeconomic (PE) studies for the product?	Yes	No
D.2 Are copies of all summarized studies included in the submission package?	Yes	No
D.3 Have you justified the relevance of these PE studies for this population?	Yes	No
D.4 Have you provided an electronic spreadsheet summary of the PE studies?	Yes	No
D.5 Will a disease or care management strategy be employed with the introduction of this product?	Yes	No
D.6 Is documentation on this intervention program included in the submission?	Yes	No

E. ECONOMIC MODEL		
E.1 Are the model structure, data and assumptions transparent and clearly presented for a non-economist reader?	Yes	No
E.2 Is an unlocked spreadsheet version of the model included with the submission?	Yes	No
E.3 Are the results presented in a style suitable for [- -] formulary committee evaluation?	Yes	No

## TERMS AND DEFINITIONS

**Care pathways:** A general method of using predetermined, time-staged, evidence-based actions for managing the care of patients who have clearly defined diagnoses or require certain procedures. Ideally, care pathways should be applicable to the management of patients moving among a managed health care system's multiple levels of care and practice settings. Other terms for care pathways include clinical care plans, clinical pathways, critical pathways, care guides, and care maps.

**Dossier:** A detailed report (in paper and electronic form) for each product submitted by the manufacturer for consideration that contains (1) clinical and economic data from published and unpublished studies and (2) a disease-based economic model to project the potential impact that introducing the product would have on health and economic consequences occurring across the entire system.

**Effectiveness:** The actual effects of treatment by the drug under "real life" conditions [patients not always remembering to take their doses, physicians often not prescribing the lowest FDA-recommended doses, side effects not all controlled, etc]. 'Head to head' effectiveness studies with similar medications are preferable.

**Efficacy:** The potential effects of treatment by the drug under optimal circumstances [e.g., patients all taking their doses at the right times, physicians prescribing FDA-recommended doses, side effects appropriately monitored, etc]. Efficacy studies are typically the foundation of new drug submissions to the FDA. Studies that compare the efficacy of similar drugs, rather than just efficacy compared to placebo are preferable.

**Formulary:** A periodically updated list of medications, related products and information, representing the clinical judgment of physicians, pharmacists, and other experts in the diagnosis and/or treatment of disease and promotion of health.

**Formulary system:** An ongoing process whereby a health care system, through its physicians, pharmacists and other health care professionals, establishes policies on the use of drugs, related products and therapies, and identifies drugs, related products and therapies that are the most medically appropriate and cost-effective to best serve the health interests of the patient populations of the health systems it represents.

**Modeling:** A quantitative modeling method used to estimate the impact of formulary changes on: 1) potential health outcomes; 2) total costs of drug and medical care in a population. One possible use of cost and outcomes modeling, for example, is to extrapolate trial-based efficacy data into effectiveness and cost-effectiveness endpoints of relevance to health care systems. Cost and outcomes impact data from models can then be used to assess the health and overall fiscal consequences of formulary changes.

## REFERENCES

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- <sup>2</sup> Task Force on Principles for Economic Analysis of Health Care Technology, Economic Analysis of Health Care Technology, *Annals of Internal Medicine*, 1995; 123:61–70
- <sup>3</sup> Hillman AL, Eisenberg JM, Pauly MV, Bloom BS, Glick H, Kinoshian B, Schwartz JS. Avoiding bias in the conduct and reporting of cost-effectiveness research sponsored by pharmaceutical companies. *N Engl J Med* 1991; 324:1362–5.
- <sup>4</sup> Agro KE, Bradley CA, Mittmann N, et. al. Sensitivity analysis in health economic and pharmaco-economic studies: an appraisal of the literature. *PharmacoEconomics* 1997; 11(1):75–88.
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- <sup>6</sup> Drummond MF, Stoddart GL, Torrance GW. Methods for the economic evaluation of health care programs. Oxford, Oxford University Press, 1987.
- <sup>7</sup> Glick H, Kinoshian B, Schulman K. Decision analytic modeling: some uses in the evaluation of new pharmaceuticals. *Drug Information Journal* 1994, 28:691–707.
- <sup>8</sup> Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-Effectiveness in Health and Medicine. New York, NY, Oxford University Press, 1996.
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- <sup>12</sup> Sheldon TA. Problems of using modeling in the economic evaluation of health care. *Health Econ* 1996;5:1–11.
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- <sup>14</sup> Mather DB, Sullivan SD, Augenstein D, Fullerton DS and Atherly D. Incorporating clinical outcomes and economic consequences into drug formulary decisions: a practical approach. *Amer J Man Care* 1999; 5(3):277–285.
- <sup>15</sup> *Principles of a Sound Drug Formulary System*. consensus document. October 2000. <http://www.amcp.org/publications/drugformulary.pdf>
- <sup>16</sup> Drummond M. Should commercial-in-confidence data be used by decision makers