McKesson Corporation

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Public Affairs

[redacted]

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McKESSON
Empowering Healthcare

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments on Risk Management Programs Concept [Docket No. 02N-0528]

Dear Sir or Madam:

McKesson Corporation (hereafter "McKesson") appreciates the opportunity to provide comment on the *Risk Management Programs Concept Paper* (docket number 02N-0528) published by the Food and Drug Administration ("FDA") on March 7, 2003. McKesson commends the Administration's efforts to seek industry input on the design of a risk management program in an effort to maximize the benefit and reduce the risks associated with the use of pharmaceutical and biotechnology products. This is an important step toward improving patient safety, while facilitating the appropriate introduction of new, life-saving therapies.

We attended FDA's April 10, 2003 Risk Management Public Workshop and noted with great interest the breadth of stakeholders and their comments regarding the FDA's risk management initiatives. As the FDA has noted, a risk management program can be designed to either *facilitate* or *constrain* the target audience. It has been our experience that it is important to maintain an appropriate balance between these two techniques to facilitate optimal patient care. We agree that the primary focus of these tools is prescribing physicians, dispensing pharmacies and patients. However, we believe it is also important to consider the role other healthcare delivery system stakeholders including payers, pharmacy benefit managers ("PBMs"), pharmaceutical distributors, other healthcare professionals have in improving patient outcomes. Their requirements should also be evaluated whenever possible to promote an optimal implementation.

McKesson is a *Fortune* 20 corporation and the world's largest healthcare information technology and services company. McKesson provides a full range of supply management solutions and information technologies that are designed to improve performance across the entire continuum of healthcare. Our market-leading businesses include healthcare information systems; patient services such as patient assistance, patient resource centers, and disease management programs; pharmaceutical and medical-surgical distribution; automation; healthcare information systems; and medical management products and services. As one of the largest nationwide distributors of pharmaceuticals and medical-surgical products to pharmacies and other health care providers, we serve as the interface between the pharmaceutical manufacturing and retail

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pharmaceuticals and medical-surgical products to pharmacies and other health care providers, we serve as the interface between the pharmaceutical manufacturing and retail pharmacy community. McKesson's Health Solutions subsidiary occupies a unique position in the pharmaceutical care system. Working in conjunction with patients, physicians and dispensing pharmacy providers, this division provides services related to the manufacturer and distribution components of pharmaceutical care delivery. In addition, this group coordinates programs and services with a broad array of payers, PBMs and other fiscal intermediaries to coordinate various reimbursement-related services for pharmaceutical and biotechnology products.

Our unique footprint in healthcare and broad array of industry touch points offers us a unique perspective of the healthcare system and how technology can be deployed to meet the needs of all stakeholders. We understand the diverse platform that is required for more effective program administration and data collection and have first hand understanding of how an effectively designed risk management program can improve patient care. Our experience includes the design and operation of managed distribution and patient support programs for beta interferon, human growth hormone, etanercept and alpha interferon at various stages of clinical development and post-approval. Each of these products and their corresponding programs were unique, with unique storage, distribution, product administration, reimbursement and patient support needs.

McKesson offers these comments based upon our firsthand experience with those program components that work well, and the dramatic impact of seemingly minor details on effective program administration.

1. Risk Management Concepts (Sect. II, lines 16 – 35 – page 2)

We agree with the FDA comments that optimizing the benefit / risk balance associated with patient drug use is a continuous learning process. Our cumulative experience with providing managed distribution systems for biopharmaceutical manufacturers over the past ten years has proven invaluable in the design and administration of subsequent programs. We encourage the FDA to continue to seek out the experience of other stakeholders. Changing program dynamics often require a quick implementation of appropriate interventions. Although new biotechnology products have revolutionized the treatment of several diseases over the past decade, our daily patient interactions suggested early on that a comprehensive program for patient training in self-injection was critical in removing this barrier to initiation of therapy. Interestingly, these improved techniques result in reduced adverse reactions, improved compliance and persistency, and ultimately patient outcomes. By taking a drug-by-drug, program-by-program approach, unique patient and program needs can be considered and often accommodated.

2. Comprehensive, Coordinated RM Planning (Sect. II, lines 40 – 45 – page 3)

McKesson shares the FDA vision of a comprehensive approach to risk management planning which also includes good risk assessment practices during the clinical development phase, and appropriate pharmacovigilance practices and assessment of observational data. While we are not offering specific comments to these concept papers, we echo the comments voiced by several meeting participants that these initiatives, while

distinct in their design and overall goals, should be integrated whenever possible. We believe one key to addressing this challenge of coordinated risk management planning is to clarify how a technological approach and comprehensive, flexible, platform design can support both the varied needs of successful drug risk management programs and the broader risk management planning process. While, as noted by one speaker, the RM tool could be viewed as the "Achilles Heel" of the FDA's risk management initiatives, we believe it can also serve to unify these three distinct program components. This framework not only provides needed direction to pharmaceutical and biotechnology manufacturers; it can also be helpful in the risk assessment phase by clarifying how a given tool or intervention might be operationalized and deployed. Such a tool could be an invaluable resource in the transition of a product from Phase III clinical studies to Phase IV surveillance. Likewise, this tool could also provide a framework for identification of product safety signals and development of a pharmacovigilance platform.

3. Human/Institutional Factors (Sect. II, starting line 76 – page 3)

McKesson's experience is consistent with the FDA's belief that a risk management program should consider critical processes, behaviors and human factors of targeted stakeholders.

Patient

Our experience suggests factors such as patient education, language and socioeconomic background are critical factors in the success or failure of therapy. For example, a risk management program will be more effective in influencing compliance for a Spanish-speaking patient if the program has integrated Spanish-speaking nurses that can communicate effectively with the patient. Similarly, nurses trained in methods of communicating at varying levels of sophistication will be more effective in influencing compliance of patients from different educational backgrounds.

Physicians

It is important to consider the varying processes, behaviors and practice infrastructure of prescribing physicians. For example, physician office training of patient self-injection is less commonplace with neurologists, which usually do not have appropriate support processes or personnel, than with endocrinologists who will often train diabetics regarding insulin injections. Similarly, the desired communications channel might differ between a busy infectious disease physician and a research-based geneticist in a teaching setting that treats rare genetic disorders.

Pharmacies
The most effective method of communicating with various types of pharmacies differs, and it is important to understand these dynamics to ensure a consistent message. Chain pharmacies, for example, tend to have centralized methods of communication, and the most effective way to communicate to these providers is often through the corporate chain headquarters. Likewise, a blast fax may be a more rapid and effective means of communicating critical information to independent community pharmacies.

4. Current Risk Management Program Tools (Sect. III, lines 175 – 213 – page 6)

The FDA concept paper describes and categorizes many of the tools that are currently in use to promote the safe use of drug products. While acknowledging FDA authority and responsibility for the ultimate selection and implementation of risk management tool(s), we submit our perspective regarding some of these existing interventions.

Education and Outreach
As noted earlier, effective communications to healthcare professionals and patients must take into consideration the diversity of these audiences, their frame of reference, potential language barriers, differences in physician specialties, practice settings and socioeconomic factors. Our experience suggests that multiple methods of communication are necessary to effectively reach physicians, pharmacies and patients. In addition, use of more than one communication channel (phone, facsimile, web, print) increases the likelihood of reaching the intended audience.

Passive Prescribing & Dispensing Controls
The use of patient agreements and documentation of informed consent are useful tools that help promote better patient understanding and attenuate the risks associated with the use of a drug. Ideally, these records should be maintained in a centralized, electronic repository where they can be readily accessed, verified and updated as required, rather than a decentralized, paper-based file in each prescribing physician's office. This is of even greater importance today with the implementation of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) and its associated requirements. McKesson's experience includes multiple programs requiring the enrollment of patients, prescribing physicians and dispensing pharmacies, and we can attest to the wealth of information that can be obtained when these processes and enrollment data are integrated with electronic systems that authorize and capture key dispensing event data (prescribing physician, patient, pharmacy, quantity, days supply and refills).

Restricted Access Systems
While restricted access systems are highly effective in enforcing compliance with a risk management program, McKesson endorses an approach that allows participation by any dispensing pharmacy provider willing to meet the terms and conditions of program participation, rather than a system that uses a single or limited number of pharmacy providers. We believe that a risk management tool that incorporates broad pharmacy access removes a potential barrier to patient use by improving patient access, and

promotes greater continuity of care by allowing patients to use the pharmacy of their choice for all of their pharmaceutical needs.

5. Effective RM Tools (Sect. III, line 225 – 240 – page 7) Lines 229 – 231

We agree that it is important to consider input from key stakeholders, such as those identified in the Concept Paper (Sect. III, lines 229 – 230 - page 7), on the feasibility of implementing and accepting the tools in usual healthcare practices, disease conditions, or lifestyles when choosing the most effective tools. We would like to add that the varied nature of these stakeholders' respective practice settings should also be considered.

Varying types of pharmacies, such as mail order pharmacies, specialty pharmacies and infusion pharmacies will have unique processes and requirements. A risk management protocol incorporating quantity restrictions of a 30-day supply will not impact a traditional retail pharmacy setting, but does not fit into the standard processes and prescription plan designs of mail order pharmacies whose business model is based upon dispensing larger quantities.

Similarly, protocols, processes and requirements differ by various third party payers, such as commercial healthcare insurers, managed care organizations, Medicaid, Medicare and other federal programs such as Department of Defense and Veterans Administration. A risk management program that impacts Medicaid patients must coordinate Medicaid pharmacy provider services in each of the 50 states.

Lines 232 – 233

We agree with the FDA's assessment that the most effective tools will be consistent with existing tools that are familiar to and accepted by targeted groups. We believe it is important that a risk management program not disrupt the daily processes that the target groups already have in place. For example, while the internet may generally be an effective medium of disseminating information, many pharmacies are either not internet enabled, or do not regularly utilize the internet. Therefore, a tool that relies upon pharmacists to electronically capture or record information via the communication channel may be less effective than alternative methods.

Lines 236 – 238

We agree that documented evidence of effectiveness that supports rationale, design, or method of use should be considered in choosing the most effective tool. As described earlier, a patient injection-training program offered through skilled nurses was found to result in fewer adverse reactions and increased patient compliance.

Line 239

We believe that a well-designed platform of RM tools will reduce the program variability and increase the repeatability of desired results. As several speakers noted during the FDA Workshop, many existing RM tools such as "sticker programs" are viewed by stakeholders as cumbersome, labor intensive and time consuming. It is our view that a more effective tool would reduce reliance upon such paper-based systems and would deploy information technology to simplify administration. Equally important, an

information technology system would generate valuable information at the physician, patient, product and dispensing level for FDA and manufacturers' use. Such a technology platform approach would have the flexibility to incorporate varied interventions or tools that are needed for a particular product.

6. Risk Management Program Categorization (Sect. III, lines 253 – 260 – page 7)

McKesson commends FDA's proposed approach to assigning levels of risk management for biopharmaceuticals to promote patient safety. We believe such a program would, where appropriate, accelerate the product approval process and promote the introduction of new, novel therapies used to treat life-threatening illness, while addressing the important issues surrounding patient safety. While we understand biopharmaceutical industry concerns that a RMP leveling system might result in a stigma associated with the product, this risk is significantly over-shadowed by the substantial increase in patient safety.

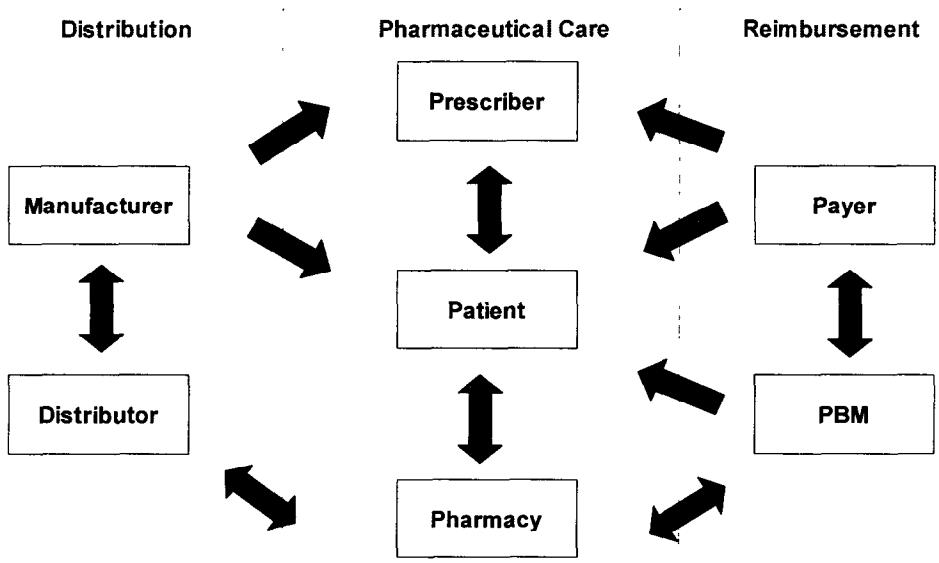
7. Evaluation Methods (Sect. III, lines 366 – 384 – page 10)

McKesson's experience with collecting adverse event data and claims data supports FDA's concerns regarding strengths, weaknesses and merits of different evaluation methods. First, McKesson's experience emphasizes the importance of differentiating between stimulated and non-stimulated adverse events. For example, a call center scripting system that manages communications to patients will avoid inadvertent stimulation of adverse event reports and maintain message consistency.

Second, we are familiar with the limitations of relying upon fragmented sources of claims data. For example, purchased claims files constitute a limited universe of patient data. Through our experience administering pharmaceutical managed distribution programs, we have learned the tremendous value of rich patient data generated by an independent, fully inclusive and all encompassing database. The database generated by such a program provides a robust source of information for the ongoing management, evaluation and revision of a risk management program.

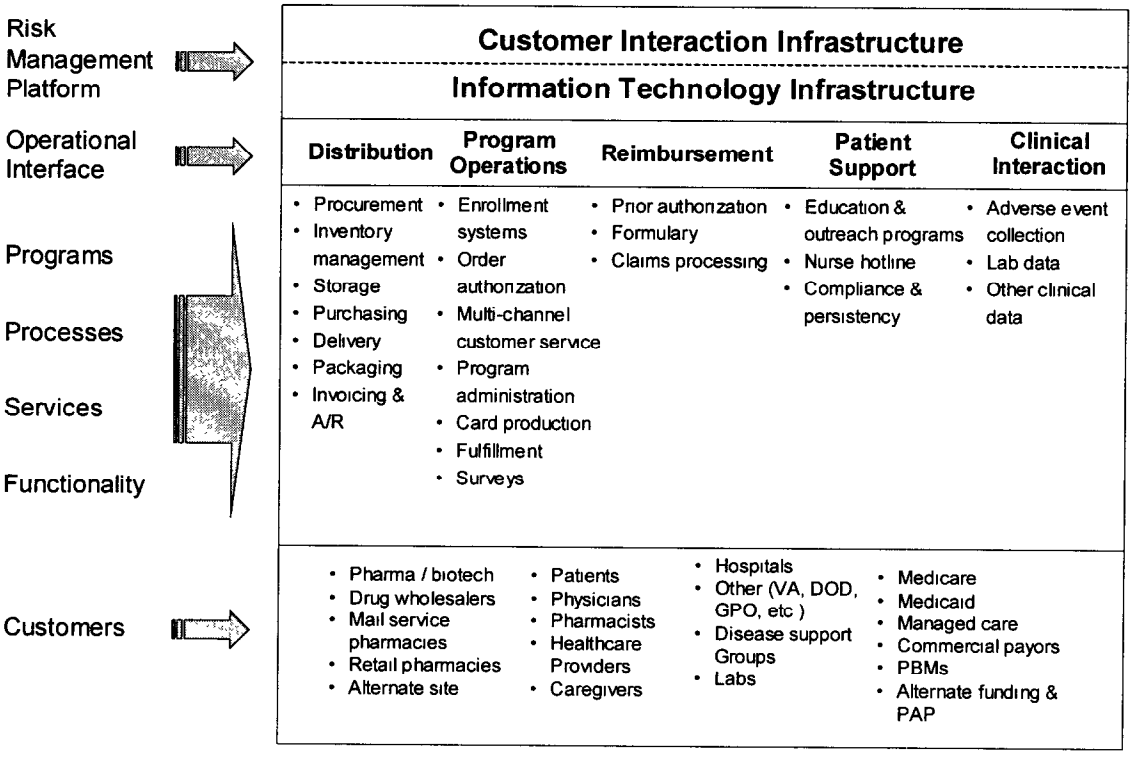
McKesson envisions a flexible, technology-based platform from which various risk management tools can be deployed to meet the unique program objectives that will invariably be associated with each drug product. From this platform, we believe customized, comprehensive, integrated and inclusive risk management tools can be designed and implemented as the need arises to effectively work within the complex U.S. healthcare system. The following diagram, while depicting a somewhat oversimplified system of the pharmaceutical care system, illustrates this concept:

Figure 1



While any risk management program must focus primarily on the pharmaceutical care component of this model, it is also important to consider associated distribution and reimbursement processes. Varying policies and requirements of Medicare, Medicaid, managed care and commercial insurers must be considered. Risk management tools for products covered under an outpatient prescription drug benefit administered by a PBM will have different considerations than those products covered under a major medical benefit. A program that limits dispensed quantities to monthly supplies, while easily accommodated in a community pharmacy setting, conflicts with normal mail service pharmacy routines that dispense three-month supplies. Likewise, each of these dispensing pharmacies has differing drug purchasing and distribution processes and relationships. Under most circumstances, this distribution component must be coordinated with one of the dozens of pharmaceutical wholesalers from which a pharmacy selects as their prime vendor for drug purchases. Similarly, some programs may not interact with traditional dispensing pharmacies, based upon the distribution channel and site of care. For example, a risk management tool associated with a product that is administered via infusion in a physician's office or alternate care facility will have different characteristics than a tool associated with a drug ordinarily dispensed in a community pharmacy setting.

Figure 2



As illustrated in Figure 2 above, one way to conceptualize this risk management platform and its associated toolbox of interventions is to view it from a technology infrastructure, the requisite operational interfaces within the pharmaceutical care model, and the programs, processes, functionality and services that are associated with these various integration points.

Figure 3

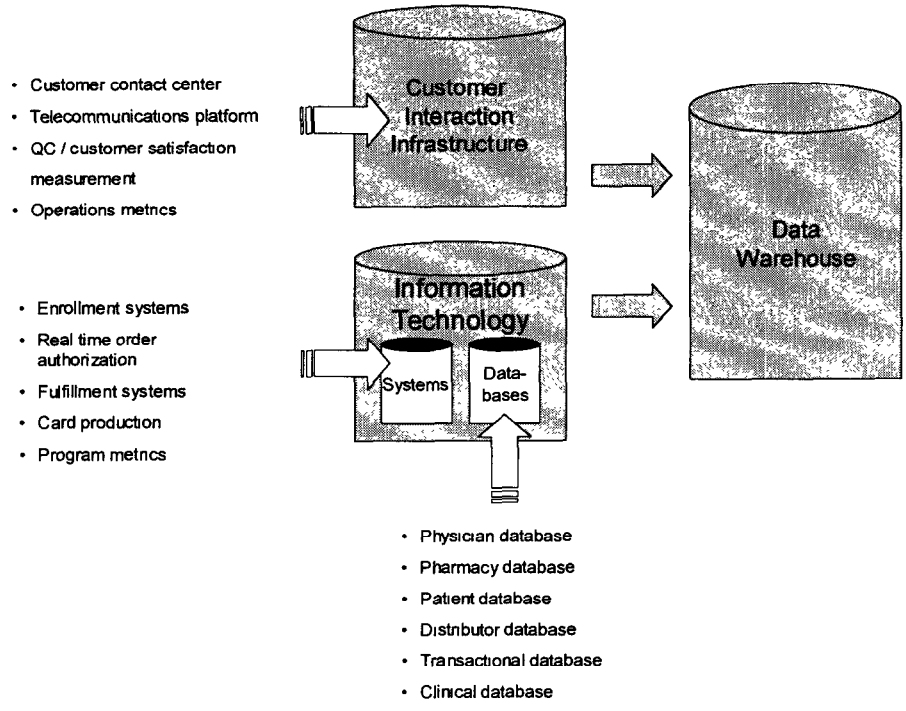
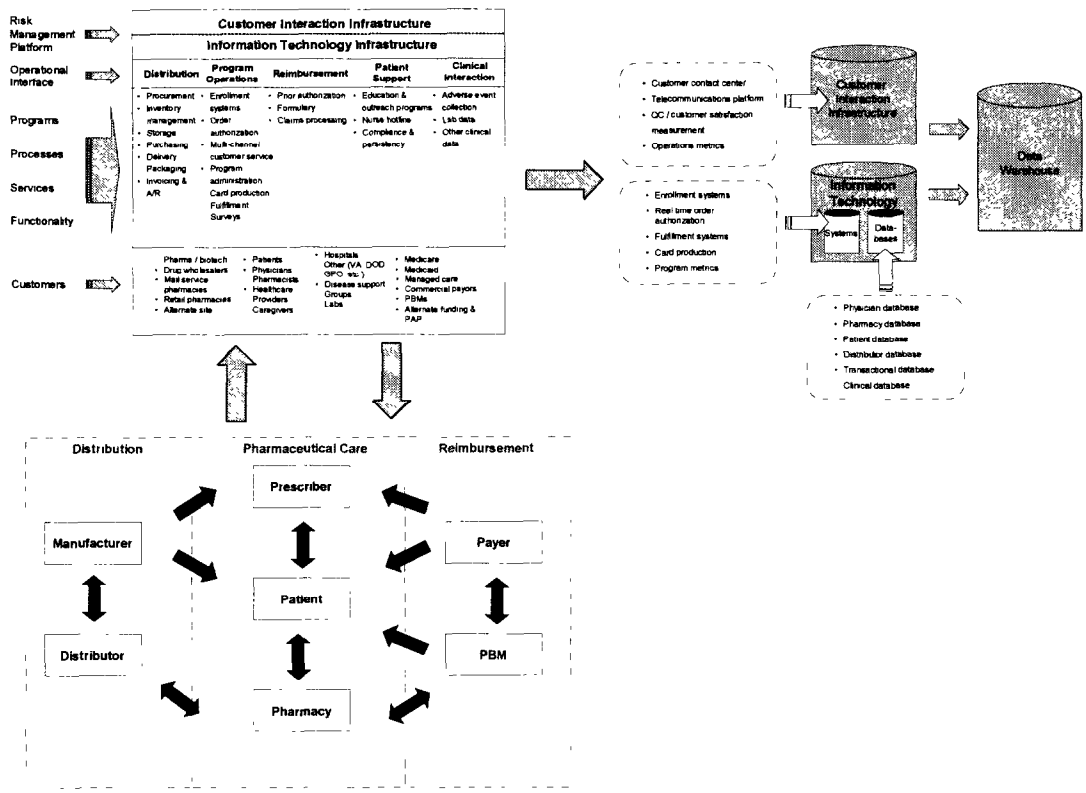


Figure 3 illustrates with greater detail the technology infrastructure and some of the systems, databases, services and metrics that could be associated with a risk management program. One key result of this approach is an integrated data warehouse that can become a stepping-stone to a complete clinical surveillance and evaluation tool.

Figure 4



McKesson appreciates the opportunity to comment on FDA's Risk Management Concept Paper. We are pleased that the Administration is taking appropriate steps to improve patient safety, while considering the unique risk / benefit profiles of pharmaceutical therapies. We believe that a technology based, inclusive risk management program that accommodates the practice settings, systems, operations and processes of the various stakeholders in the pharmaceutical care system will most effectively achieve this objective.

Although no model currently exists, much of the technology and infrastructure exists and is operating today. We believe that a platform as depicted above can also assist in the critical task of a completely integrated risk management solution, inclusive of risk assessment and pharmacovigilance. McKesson stands ready to assist the Administration and the healthcare industry in accomplishing these risk management initiatives.

Sincerely,

Ann Richardson Berkey