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Resource Evaluation of the FDA Food Additive Petition Process

Executive Summary

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Prepared by

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Executive Summary

INTRODUCTION

In 1958, Congress passed the Food Additives Amendment to the Food, Drug, and Cosmetics Act requiring the Food and Drug Administration's (FDA's) premarket approval for food additives prior to inclusion in food. Premarket approval is sought via the petition process. The statute requires that FDA complete its petition review within 90 days of filing, with a possible extension of another 90 days and an extended processing period of 180 days. However, FDA has been unable to consistently meet these statutory time frames. Critics have charged that the process needs improvement, although some concede that the statutory time frames are unreasonable given FDA's resources and the competing demands on those resources.

FDA has sought to improve the petition review process and expedite petition review, but no studies have quantified the actual resources required for each of the Office of Premarket Approval's (OPA's) various responsibilities or detailed the impact of competing requirements on the petition review system itself. Performing these analyses was the objective of Research Triangle Institute's (RTI's) project for FDA's Center for Food Safety and Applied Nutrition (CFSAN).

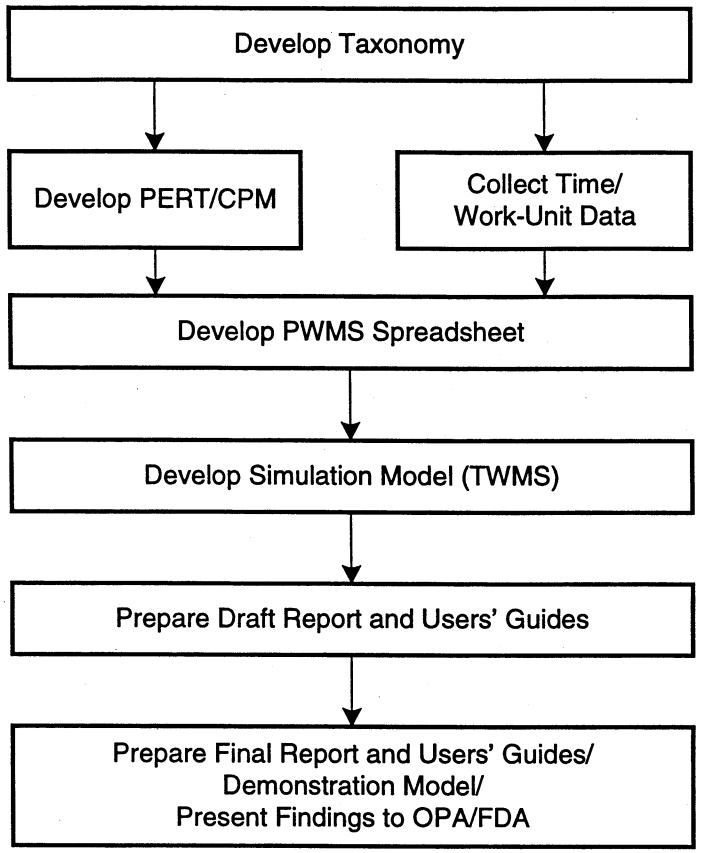
submitted petitions. CFSAN expects these trends to continue due in part to new developments in areas such as biotechnology and recyclable food packaging.

In addition to the increasing number and complexity of submissions, OPA personnel perform a myriad of other duties such as responding to inquiries from industry and Congress, developing submission and scientific review guidelines, and participating in FDA policymaking. With increasing international trade, CFSAN also anticipates requiring OPA personnel to assist with the international harmonization of food additive standards.

METHODOLOGY

RTI used an interdisciplinary approach in its analyses of the petition review process, combining our capabilities in systems analysis, operations research, economics, toxicology, chemistry, environmental science, and data quality analysis. Figure 1 illustrates our approach. With information and advice from OPA, RTI developed a taxonomy—names and brief definitions—of the essential work units required to review current and future petitions as well as OPA tasks and responsibilities that are not directly related to a filed petition. Based on this work-unit taxonomy, we gathered information concerning the types of personnel, level of effort by personnel type, and any other resources required to complete the various work units. Petitions were classified into three tiers according to the number and complexity of their work-unit components. Each tier was then further subdivided into classes of petitions depending on the amount of review material submitted and the overall estimate of review duration. Combining this information on petition classification, work units, and resource requirements, we designed and delivered two IBM/PC-compatible software products: a Petition Workload Measurement System (PWMS) and a Total Workload Measurement System (TWMS).

Figure 1. Flow Diagram of Project Approach



and tasks that have to be performed consecutively. The main strength of the PWMS is its focus on the details surrounding a single petition. It provides an immediate estimate on the types of personnel, personnel time, and calendar time required to review a single petition of a given petition type without competing priorities.

The TWMS, created in the simulation software ProcessMod, is a simulation model generated from the process flow diagrams of the three tier levels detailed in the PWMS. To perform a simulation, the TWMS is run for a period of time during which petitions enter the system to be reviewed. Along the specific path each petition

The TWMS permits the user to develop a sense of the entire system of petition processing at OPA. It provides a view of the different types of petitions that arrive, the different review times that each petition will require, personnel constraints, and competing priorities. Because it incorporates much of the randomness present in these factors, it provides a better sense of the real-world functioning of OPA petition review than a static model would provide. It is possible to determine the average amount of time it takes for a petition to be processed, including the amount of this time that was spent under active review and the amount of this time that was spent waiting. The TWMS shows graphically where the back-ups in petition processing occur and their possible causes. The TWMS also provides information on resource use by highlighting over- and underused resources.

RESULTS

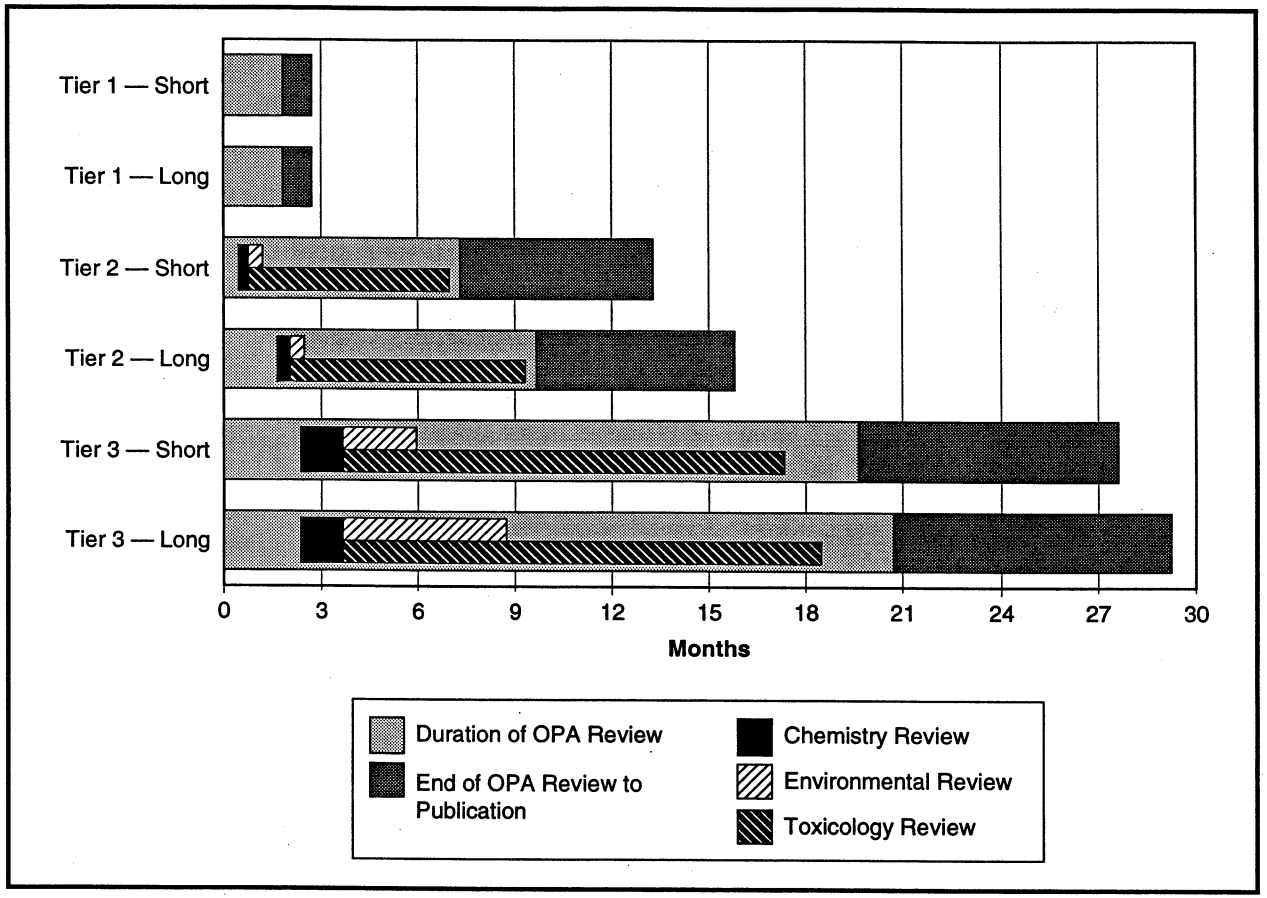
The results obtained from our systems analysis are described below.

PWMS Results

Figure 2 provides, by tier level and amount of review material (short or long), a sense of the calendar time required by the different components of the full petition review process. The results are shown for average duration petitions.

The time required to completely process Tier 1 petitions is 2 to 3 months after their arrival at OPA. Tier 2 petitions are usually processed in about 1 year of their arrival at OPA, though some may take up to 2 years. Tier 3 petition review time averages 2.5 years, but the range is wide, from 1.75 years to 3.5 years. Recall that these time estimates do not include delays caused by petitioner response times to amendment requests. Any amendment request that is not immediately answered substantially delays the review process.

Figure 2. Length of Calendar Time to Complete Petition Review Components with Respect to Total Petition Review Time



are great for Tier 2 petitions and even greater for Tier 3 petitions. Toxicology review is by far the largest (and longest) single piece of the petition review process. The total petition processing times vary somewhat within Tier 2 categories, but this phenomenon is much more pronounced within the Tier 3 categories. Very large differences are visible between the high and low durations within tier categories. Tier 3 petitions have the widest range in petition processing times, both at the component level and the overall

duration level), and Tier 3 petitions could be completed up to 2 months faster. Given the magnitude of review time required, these changes are very small. Since the impact of staggering reviews is so minor, staggering the scientific reviews does not greatly affect the model results. The lower bound on the amount of petition review time required for petitions is primarily driven by the toxicology review.

It is also apparent in Figure 2 that post-OPA petition processing can add a substantial amount of time to the process as a whole. In addition, this extra time is beyond OPA's control.

The major tasks on the critical paths for the three tiers are discernible from the lengths of the shaded bars from Figure 2 as well. The critical path for each tier is as follows:

Tier 3—chemistry review, toxicology review, and Level 2 toxicology studies.

Tier 2—chemistry review, toxicology review, and Level 1 toxicology studies.

Tier 1 (all except long-high petitions)—*Federal Register* notice, 30-day comment period.

Tier 1 (long-high petitions)—special project team (SPT) chair set-up activities, toxicology review, and SPT collection and draft rule.

Figure 3 shows the actual hours required for petition review by personnel category (measured in terms of hours of review time, not calendar time) required for petition processing by personnel category for each petition category for Tier 2 and Tier 3 short (amount of review material) average (duration) petitions.

Complementing Figure 3, Table 1 compares the number of hours required by personnel category to complete three hypothetical bundles of petitions. The bundles are groups of 50 petitions. Bundle A corresponds to the average petition bundle. It includes 20 Tier 1 petitions, 20 Tier 2 petitions, and 10 Tier 3 petitions.

Figure 3. Actual Hours Required for Petition Review by Personnel Category

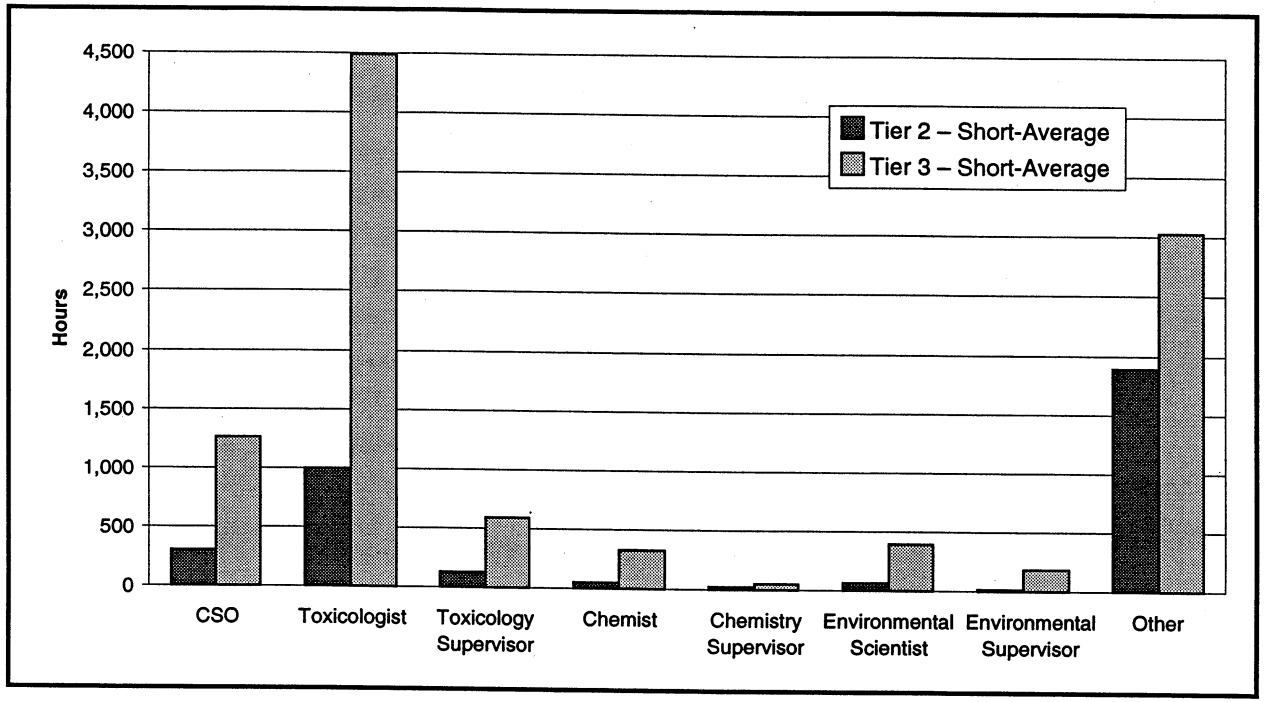


Table 1. Comparison of Petition Bundle Hourly Requirements and Personnel Availability

Personnel Categories	Hours Needed for Complete Petition Bundle Review			Hours Available in 1 Year	
	Bundle A Hours	Bundle B Hours	Bundle C Hours	Available Hours	Petition Review Available Hours
CSO	15,614	10,128	14,371	84,000	13,440
Toxicologist	67,958	29,689	49,082	38,000	16,720
Toxicology supervisor	8,549	3,501	6,076	12,000	2,520
Chemist	4,187	2,106	2,720	12,000	3,480
Chemistry supervisor	917	490	854	8,000	880
Environmental scientist	5,785	3,056	2,758	8,000	3,680
Environmental supervisor	1,890	777	1,225		

assumed that all petitions in each bundle will be accepted and approved substances.

In addition to the number of hours required by personnel category for the petition bundle review, the table contains the number of hours currently available by personnel category if all personnel were devoted solely to petition processing and the number of hours currently available by personnel category given competing demands. The available hours and available petition review hours represent the hours for 1 year. The number of hours required by personnel category to complete three hypothetical bundles of petitions was taken directly from the PWMS hourly calculation spreadsheet.

Table 1 shows that, regardless of the petition bundle chosen, there seems to be a lack of toxicologist hours available, especially when considering the actual hours available for petition review. A potential lack of toxicology supervisor hours is also apparent, implying that there are not enough hours to complete the review of the bundle in 1 year. The remaining personnel categories appear to have sufficient petition review hours available for these petition bundles within a year. Further analysis can be performed on alternate petition bundles by using the software that accompanies this report.

Comparison of Amount of Effort

As part of the Project Delivery Order, FDA requested that RTI conduct an independent assessment of the scientific labor effort required to review petitions. To meet this requirement, a panel of three RTI scientists (one toxicologist, one chemist, and one environmental scientist) was convened to examine three sample petitions that were also examined by OPA scientists and to provide their own best estimates of the time required to conduct each activity (when applicable) for each petition. After each team (OPA

Sample Petition Result" is based on consensus estimates for those activities where a consensus was reached and *RTI's* estimates for work activities where a consensus was *not* reached.

Using the OPA comparison estimates, the sample petition finishes its within-OPA review on June 8, 2000, and the response to objections after the rule has been published finishes on March 14, 2001. Using the RTI comparison estimates, the sample petition finishes its within-OPA review on July 8, 1999, and the response to objections after the rule has been published finishes on March 23, 2000. The estimates differ by about 1 year. This discrepancy is mainly due to the differences in the estimated amount of time required for the toxicology reviews. Table 2 shows the differences in duration between the two comparison estimates.

Table 2. Differences in Hourly Estimates of Task Duration

Tasks	OPA Estimate	RTI Estimate
Chemistry information	42	11
Level 1 toxicology studies	1,166	572
Level 2 toxicology studies	1,506	919
Level 3 toxicology studies	591	678
Review of the amendment	3,915	2,602
Subsequent supervisory review	392	260
Acceptable daily intake (ADI) evaluation	18	49
Total for these tasks	7,630	5,091

The difference of 2,539 hours between the two estimates translates into an 11-month difference in the amount of time for OPA to complete its petition review.

Note that both of the "Sample Petition" PWMS model illustrations

TWMS Results

We decided to run the TWMS simulations over a 4-year time horizon. To ensure that the model results were not biased because of a start-up period when there are no petitions in the system, we included a warm-up period of 6 months. During the warm-up period, petitions enter the system and are processed as usual, but the simulation does not collect statistics on them. The simulation only collects statistics on petitions that have entered the system after the warm-up period ends, though the petitions that entered the system during the warm-up period also remain in the system for processing. In addition, the statistics on the personnel categories (resources) and on the petition review tasks themselves (activities) are not collected until after the warm-up period is complete.

The simulation is run for ten iterations, and the statistics collected during each run are aggregated to form the average result. Full statistics are available, but we show only the average and the standard deviations for most of the results we present in this report. For the full statistics to be truly meaningful, the simulation would have to be run for far more than ten iterations.

Table 3 shows the results of our base case analysis. Roughly 50 petitions arrive each year, of which 40 percent are Tier 1, 40 percent are Tier 2, and 20 percent are Tier 3. Personnel availability for petition review tasks is restricted by competing priorities as established during our data collection effort. In the base case simulation, on average 73 Tier 1 petitions, 85 Tier 2 petitions, and 40 Tier 3 petitions were submitted within a 4-year period.

Table 3. Petition Processing Results

Petition Type	Quantity Processed (Standard Deviation)	Average Processing Time (months) (Standard Deviation)
Tier 1 (SPT)	46.00	4.5
	(7.04)	(1.0)

Table 3 shows the average results of our simulations in terms of the number of petitions processed and the calendar length of time it took to process them entirely. For the purposes of this model, 2,000 hours roughly equal 1 year. Therefore, Tier 1 petitions (SPT petitions) are processed in roughly 4.5 months. Tier 2 petitions (routine petitions) are processed in just over 2 years. Tier 3 petitions (complex petitions) are processed in just under 3 years. During the 4 years, 46 Tier 1 petitions, 15 Tier 2 petitions, and 5 Tier 3 petitions were processed on average.

These results indicate that the times for processing petitions were not unreasonable. To explore these results further, we examined an animated simulation of the TWMS. Examining the animation, we see delays forming in tasks where petitions are backing up (seen by a growing queue). The delays occur in the chemistry supervisory review activities, the supervisory review activities in environmental review, and toxicology in general. The delays occurring in the chemistry supervisory tasks are substantial and affect the speed of petition processing. In addition, these delays may cause chemistry reviewers to wait on petitions, thus forcing their percent utilization to be lower than their availability. The simulation also exposes delays in the environmental supervisory tasks, but they do not delay the actual petition processing time since their review finishes faster than the toxicology review. The delays in the toxicology review are substantial. This problem is compounded by the fact that the toxicology review is the longest single review, as demonstrated by the PWMS. Therefore, it is not unusual for all other reviews to finish before the toxicology review is complete. This fact is illustrated in the animation by petitions remaining in Level 1 or Level 2 studies for Tier 2 and Tier 3, respectively. The animation reveals large delays (not related to actual petition processing efforts) in tasks requiring toxicology supervisors. In fact, these delays are so large that they cause toxicology reviewers to wait because the supervisors need to perform their petition review tasks before the

The TWMS can be used to explore several other scenarios such as

- the base case at 10 years;
- the case where there are no availability restrictions on personnel (in this case, the constrained resources arise only because of competition between multiple petitions);
- different staffing options;
- different petition arrival rate; and
- different tier composition of arriving petitions.

The results of these alternate scenarios are presented in our report.

CONCLUSIONS

Statutory Time Frames

Only Tier 1 petitions can reliably and predictably be processed within the 180-day statutory time frame. The PWMS shows that without competing priorities Tier 1 petitions are normally processed within 2 to 3 months. The TWMS shows that even with competing priorities SPT petitions can normally be processed in about 120 days.

Neither Tier 2 nor Tier 3 petitions can be reviewed within the 180-day statutory time frame, even without competing priorities. The PWMS shows that given the ordering and duration of tasks it is not feasible to review Tier 2 or Tier 3 petitions within 180 days, regardless of OPA staffing levels. For this statutory time frame to be feasible, the entire review procedure and the amount of information and material required for review would have to be drastically altered.

Some Tier 2 petitions can be reviewed within the 360-day extended processing period. In particular, the Tier 2 short-low petitions (i.e., petitions that contain no extra studies and are well prepared and without complications) can be reviewed within 360 days according

days. It is exceptionally rare for Tier 2 and Tier 3 petitions to be amendment free.

Given current personnel, even if all of their time and efforts were dedicated to reviewing filed petitions (i.e., there are no availability constraints), the average review period for Tier 2 petitions is 18 months. Our base case with personnel availability constraints predicts an average of slightly more than 2 years for a Tier 2 petition to be processed. The TWMS predicts the time required to process subsequent petitions will increase steadily.

Tier 3 petitions cannot be reviewed within the 360-day extended processing period, even without competing priorities. The PWMS shows that given the ordering and duration of tasks it is not feasible to review these petitions in that time regardless of OPA staffing levels. The minimum processing period predicted by the PWMS for Tier 3 petitions is 1.5 years, but the *average* processing period is about 2.5 years, with difficult ones taking up to 3.5 years. Given current personnel, even if all of their time and efforts were dedicated to reviewing filed petitions (i.e., there are no availability constraints), Tier 3 petitions would be processed on average in 2 years. Our base case with personnel availability constraints predicts an average of slightly more than 2.75 years for a Tier 3 petition to be processed with a steadily growing delay. The TWMS predicts the time required to process subsequent petitions will increase steadily.

The sensitivity analyses of the TWMS reveal that Tier 3 petitions have a very large impact on how well the entire petition review process functions. Even "normal" Tier 3 petitions require substantial personnel resources, and if several of these petitions are in the system at once, the review times of petitions in all tiers are adversely affected.

We conclude that the statutory time frames are unrealistic for all petitions except Tier 1 petitions. The ability to meet these time