GRAS Review Time Technical Report

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Abstract

Background. In August 2026, the U.S. Food and Drug Administration (FDA) proposed making notification mandatory for substances used in food on the basis of a generally recognized as safe (GRAS) conclusion. FDA's Preliminary Regulatory Impact Analysis (PRIA) projects about 98.5 additional full notices per year and several thousand one-time streamlined submissions. It does not estimate elapsed review time or the capacity needed to meet the program's response timeline.

Methods. All 1,360 human food notices in FDA's GRAS Notice Inventory (1998–2026) were classified into 15 ingredient classes by two independent coding passes and a manual check. Receipt and filing dates missing from the Inventory after about 2017 were recovered from 642 FDA response letters. Time from receipt to response was estimated by Kaplan–Meier analysis with pending notices censored. A fluid queue model, parameterized with PRIA inputs, projected the added wait under the proposed rule at several levels of review capacity.

Results. The median wait from receipt to filing rose from 22–35 days (2016–2018) to 84–204 days (2020–2025). The median time from receipt to response was 289 days, and about 1% of notices received in 2025 closed within 180 days of receipt, compared with 29% in 2017. From 2021 to 2025 FDA closed about 69 notices per year, roughly equal to inflow. Median review time differed by ingredient class, from 162 days for sweeteners to 245 days for biomass and whole-cell ingredients, as did the share of notices FDA ceased to evaluate (7% to 38%). The PRIA's projected inflow would require about 2.4 times current throughput. With capacity unchanged, the modeled added wait for a full notice reaches 2.8 years in the first year and 8.5 years by the fifth.

Conclusions. The GRAS notification program already operates near full utilization, and a growing share of each notice's wait now falls before the filing date from which the response timeline is measured. Without a corresponding increase in review capacity,

mandatory notification is likely to produce multi-year delays. Measuring review time from receipt and adding a capacity analysis to the final regulatory impact analysis would make these risks visible.

Keywords: GRAS; food ingredient regulation; FDA; review time; survival analysis; queueing model; regulatory capacity

1. Introduction

Under Section 201(s) of the Federal Food, Drug, and Cosmetic Act, a substance that is generally recognized as safe under its intended conditions of use is not a food additive and does not require premarket approval. Since 1998, and under a final rule since 2016, FDA has operated a voluntary program in which a company may notify the agency of its GRAS conclusion. FDA files the notice, evaluates it, and responds, most often with a letter stating that it has no questions. Under the current regulation, FDA responds within 180 days of filing and may extend that period by 90 days (21 CFR 170.265(b)).

In August 2026, FDA proposed making this notification mandatory (91 FR 51834; Docket FDA-2025-N-3262). The proposal would also create a one-time streamlined pathway for substances already marketed under independent GRAS conclusions. FDA's PRIA estimates that the rule would add 98.5 full notices per year (range 60–137) and 6,740 one-time streamlined submissions (range 2,740–13,740). It estimates about 63 hours of FDA review per full notice and about 11 hours per streamlined submission.

Those estimates describe the effort per submission, not the time a submitter waits. Elapsed review time depends on how inflow compares with the program's throughput, and on how long notices wait before review begins. Neither quantity is reported in the PRIA, and the second is no longer reported in FDA's public Inventory.

This report asks three questions:

1. How long do notices wait between receipt and filing, and how has that wait changed?
2. How close is the program to its capacity, and how does review time differ by ingredient class?
3. What added wait would the PRIA's projected inflow produce at different levels of review capacity?

2. Data

GRAS Notice Inventory. The full Inventory was exported from FDA's website on November 2, 2026. It lists 1,360 notices (GRN 1 to the most recent) with substance, notifier, intended use, filing date, closure date and the text of FDA's response. Of these, 1,074 closed with a "no questions" letter, 226 with a cease-to-evaluate letter, 20 with an insufficient-basis letter, and 40 were pending.

Response letters. The Inventory reports filing dates only for notices up to about GRN 700 (2017) and never reports receipt dates. FDA's response letters, however, routinely state both ("We received your notice on … and filed it on …"). Letters were downloaded for every closed notice with a linked letter, and receipt and filing dates were extracted from 642 of them. Dates in cease-to-evaluate letters that refer to the notifier's cease request, rather than to receipt, were identified and excluded.

FDA's Preliminary Regulatory Impact Analysis. Inputs for the projections were taken directly from the PRIA for the proposed rule: the projected increase in full notices (98.5 per year; 60–137), the number of streamlined submissions (6,740; 2,740–13,740), FDA review hours per full notice (63) and per streamlined submission (11.03), and the count of filed notices pending evaluation in March 2025 (94 in total, 90 for human food; PRIA Table 4).

3. Methods

3.1 Ingredient classification

Each notice was assigned to one of 15 classes by what the substance is: enzymes; microbial strains; precision-fermentation proteins; human milk oligosaccharides (HMOs); sweeteners; lipids and oils; proteins; carbohydrates and fibers; botanicals; colors and carotenoids; nutrients; processing aids and antimicrobials; biomass and whole-cell ingredients; whole and minimally processed foods; and other. The codebook was written before coding and revised once, when the whole-food class was added. Processing aids were limited to substances used for machinery or mechanical-physical processing.

Two independent large-language-model coding passes classified every notice from its substance name and intended use. They agreed on 95.2% of notices (Cohen's $\kappa = 0.947$). The author reviewed all disagreements and a random sample of 150 notices; agreement between the author and the AI consensus on the random sample was 92.7% ($\kappa = 0.919$). Final codes give precedence to the author's calls, then to the AI consensus.

3.2 Date recovery and intervals

Three intervals were defined: the **pre-filing wait** (receipt to filing), **review time** (filing to FDA response), and **total time** (receipt to response). Filing and closure dates came from the Inventory where present and from response letters otherwise. Pending notices and cease-to-evaluate notices carry no receipt date. Because GRN numbers are assigned in order of receipt, their receipt dates were interpolated from GRN order. Against notices with known receipt dates, GRN order tracked receipt closely (Spearman $\rho = 0.999$; leave-one-out median absolute error 8 days, 90th percentile 58 days).

3.3 Survival analysis

Total time from receipt to response was estimated with the Kaplan–Meier method, by year of receipt. Notices still pending on November 2, 2026 were treated as censored at that date. This avoids the bias of summarizing only closed notices, which in recent cohorts are the ones that closed fastest.

3.4 Queue model

A deterministic fluid model was run in monthly steps. Review capacity was expressed in full-notice equivalents per year; current capacity was set to 69, the mean annual number of closures in 2021–2025. Baseline arrivals were also 69 per year, to which the PRIA's 98.5 additional full notices were added. Streamlined submissions arrived evenly over a 24-month window, each counted as $11/63 = 0.175$ of a full notice, the PRIA's ratio of review hours. The starting backlog was 94 notices.

Two service disciplines were modeled. In the **priority** case, full notices are reviewed before any streamlined submission, the case most favorable to full notices. In the **first-in, first-out** case, all submissions share one queue. Capacity was varied at 1.0, 1.5, 2.5 and 3.5 times current. The output is the added wait for a newly received full notice, on top of current review times.

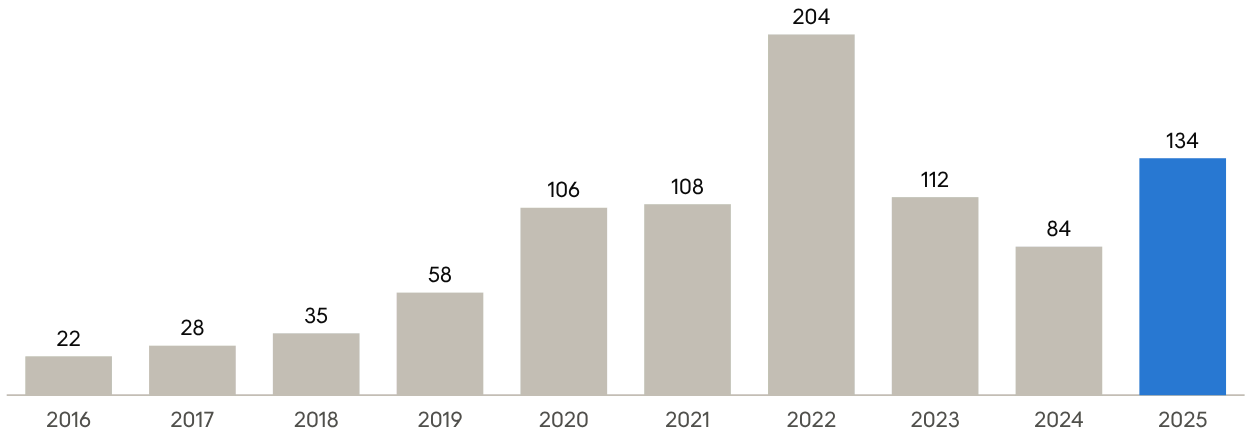
4. Results

4.1 The pre-filing wait

The median wait from receipt to filing rose about four-fold, from 22–35 days for notices received in 2016–2018 to 84–204 days for those received in 2020–2025.

Notices now wait months before review begins

Median days from FDA receipt to filing, by year received



FDA response letters (642) · notices received 2016–2025 with stated receipt and filing dates

The wait peaked for notices received in 2022 and has not returned to its earlier level. For notices received in 2023–2025, the interquartile range was 84 to 155 days (n = 160).

4.2 Total time from receipt to response

Across all dated notices, the median time from receipt to FDA response was 289 days. Kaplan–Meier medians by year of receipt were 193 days in 2017, 446 days in 2022, 251 days in 2024 and 327 days in 2025, with 20 of the 2025 notices still pending. About 1% of notices received in 2025 closed within 180 days of receipt, compared with 29% of those received in 2017. The 2026 cohort is too recent to assess.

4.3 Throughput and utilization

From 2021 to 2025, FDA filed a mean of 64 notices per year and closed a mean of 69. Inflow and throughput were therefore close to equal, which corresponds to utilization near 100%.

Year	Notices filed	Notices closed
2021	62	70
2022	61	52
2023	71	85
2024	58	64

Year	Notices filed	Notices closed
2025	68	73

Review time after filing rose with load. For notices filed in 2020–2022, the median review time was 252–293 days, and 40–54% of notices exceeded 270 days, the response period plus the full extension. Notices filed in 2024–2025 that have closed show shorter times (159–167 days), but these cohorts are right-censored: the slowest notices from those years are still pending.

4.4 Differences by ingredient class

Review time and outcome differed by class. Novel ingredients took longest and were most often withdrawn; enzymes, microbial strains and sweeteners moved fastest and were rarely withdrawn.

Ingredient class	Closed notices	Median days, filing to "no questions" letter	Share ceased to evaluate
Biomass and whole-cell ingredients	34	245	38%
Human milk oligosaccharides	61	242	10%
Proteins (conventional)	75	214	27%
Precision-fermentation proteins	23	184	30%
Botanicals	77	180	34%
Enzymes	177	178	7%
Microbial strains	158	177	9%
Sweeteners	151	162	8%

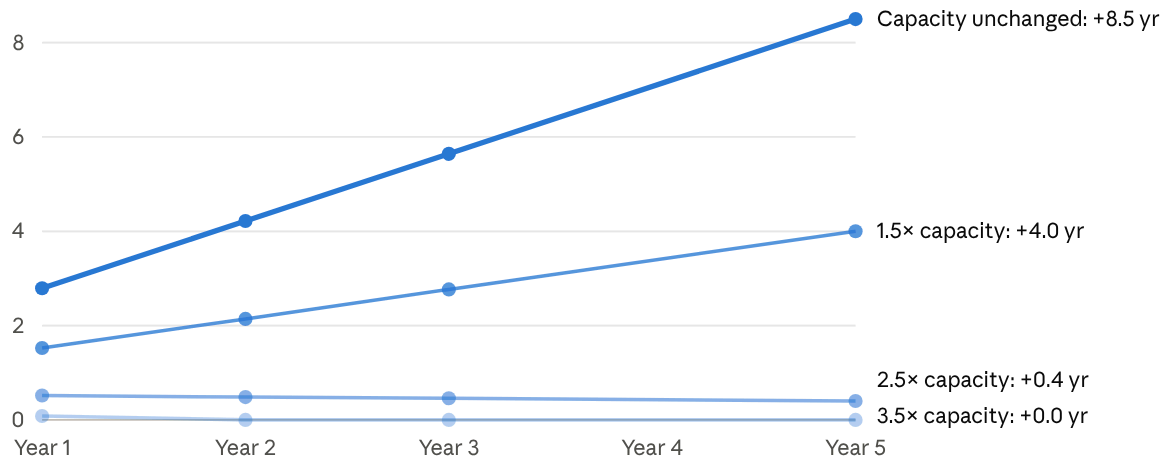
All closed notices, 1998–2026. Selected classes; the other seven classes fall between these values.

4.5 Projected queue under the proposed rule

The PRIA's 98.5 added full notices raise inflow from about 69 to about 168 per year. Capacity must therefore rise by a factor of 2.43 to keep pace with full notices alone.

With capacity unchanged, the added wait reaches 8.5 years by year 5

Modeled added wait for a new full notice, in years (full notices reviewed before streamlined submissions)



Queue model with FDA PRIA inputs · 98.5 added full notices/yr · starting backlog 94 · priority discipline

At 2.5 times current capacity, the added wait stabilizes near 5 months; at 3.5 times, the queue clears within the first year. When streamlined submissions share a single first-in, first-out queue with full notices, delays are much longer. With 6,740 streamlined submissions and capacity unchanged, the added wait for a full notice is 11.3 years in the first year. Even at 2.5 times capacity, the streamlined backlog does not clear within ten years. Starting the backlog at 40 rather than 94 notices changes these results only modestly.

5. Discussion

5.1 A wait the current metric does not see

The program's response timeline is measured from filing. The largest change over the past decade, however, occurred before filing: the median pre-filing wait grew from about a month to three to seven months. A notifier experiences the full interval from receipt. Under a voluntary program this is a commercial inconvenience. Under a mandatory program it becomes a regulatory delay borne by every company that uses a new ingredient, and it is not visible in the public Inventory, which no longer reports filing dates.

5.2 Capacity, not effort, sets elapsed time

The PRIA's review-hour estimates are plausible as measures of effort. But the median notice takes about 289 calendar days from receipt to response, against 63 estimated hours of review. The difference is waiting time. In a queue operating near full utilization, waiting time is highly sensitive to added inflow, which is why a 2.4-fold increase in full notices produces multi-year delays in the model rather than proportional ones. The model's main lesson does not depend on its precise parameters: unless capacity grows by at least the factor that inflow grows, the queue does not stabilize.

5.3 The classes most affected

The ingredient classes that now take longest to review and are most often withdrawn, such as biomass, novel proteins and botanicals, are also those most likely to have been marketed under independent GRAS conclusions without notification. Mandatory notification is therefore likely to shift the program's mix toward slower classes, which would increase average review effort beyond the PRIA's uniform 63 hours.

5.4 Limitations

- Receipt dates for pending and cease-to-evaluate notices were estimated from GRN order. The estimation error is small (median 8 days) relative to the intervals studied.
- Review times for notices filed in 2024–2026 are right-censored and should not be read as an improvement until those cohorts close.
- Classification relied on substance names and intended uses; some notices span classes.
- The queue model is deterministic and treats notices as interchangeable within each track. Its capacity multipliers are scenarios, not forecasts, and it does not represent changes in staffing practice, triage, or notice complexity.
- The count of filed, pending notices differs between FDA's internal figure (90 for human food, March 2025) and the public Inventory (40, November 2026). The model's results change only modestly between these starting values.

6. Conclusions

1. The wait between receipt and filing of a GRAS notice has grown about four-fold since 2016–2018 and is not captured by the program's filing-based timeline.
2. The program closes about as many notices as it receives, leaving no reserve capacity.

3. FDA's projected inflow under mandatory notification requires about 2.4 times current throughput; without that increase, the modeled wait grows by years.
4. Review time and outcome differ by ingredient class, and the slowest classes are those most likely to enter the program under the rule.

Measuring review time from receipt, publishing filing dates and the pending count, and pairing the rule's volume estimates with a staffing and capacity analysis would allow these risks to be managed before the rule takes effect.

Data availability

The classified notice dataset, with recovered receipt and filing dates, is available as a CSV at tools.mendocinofoodconsulting.com/gras-timeline/gras-notices-classified.csv. An interactive estimator built on these results is the GRAS Timeline Estimator, and a plain-language summary is the whitepaper. Analysis code is available from the author on request.

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