FY 2016

PERFORMANCE REPORT TO CONGRESS

for the

Animal Drug User Fee Act

Commissioner's Report

I am pleased to present to Congress the Food and Drug Administration's (FDA or the Agency) Fiscal Year (FY) 2016 Performance Report to Congress for the Animal Drug User Fee Act (ADUFA). On June 13, 2013, the second reauthorization of ADUFA was signed into law. This reauthorization of ADUFA for another 5-year period (FY 2014 through FY 2018) is referred to as ADUFA III. This report marks the third year of ADUFA III.

This report details FDA's preliminary performance for FY 2016, and finalizes performance results for FY 2015. It is my pleasure to report that FDA exceeded all performance goals for FY 2015. The Agency also met review-time goals for all FY 2016 cohort submissions reviewed or due for review by September 30, 2016. With some reviews still pending, FDA has the potential to exceed all performance goals for FY 2016.

FDA is committed to improving the efficiency, quality, and predictability of the new animal drug review process. We are dedicated to exploring new approaches and technologies that offer high-quality, cost-effective improvements in the Agency's review of new animal drug applications and submissions. Under the leadership of the President and in collaboration with Congress and industry, FDA looks forward to the continued success and significant improvements in the animal drug review process made achievable by ADUFA.

Robert M. Califf, M.D.
Commissioner of Food and Drugs

Acronyms

ADAA – Animal Drug Availability Act

ADUFA – Animal Drug User Fee Act

CBE-30 – Changes Being Effected in 30 Days

CFR – Code of Federal Regulations

CMC – Chemistry Manufacturing and Controls

CVM – Center for Veterinary Medicine

ERA – End-Review Amendment

FDA – Food and Drug Administration

FD&C Act – Federal Food, Drug, and Cosmetic Act

FY – Fiscal Year (October 1 to September 30)

HHS – U.S. Department of Health and Human Services

INAD – Investigational New Animal Drug

MUMS – Minor Use or Minor Species

NADA – New Animal Drug Application

ONADE – Office of New Animal Drug Evaluation

QLS – Qualifying Labeling Supplements

Executive Summary

On June 13, 2013, the second reauthorization of ADUFA, referred to as ADUFA III, was signed into law for an additional 5 years (through FY 2018). Following negotiations with industry as part of the reauthorization process, FDA agreed to pursue a comprehensive set of review performance goals and commitments that seek to improve the timeliness and predictability of the review of new animal drug applications (NADAs), supplemental NADAs, and investigational new animal drug (INAD) submissions.

More information on the history of ADUFA is available on the FDA website.[1]

Information Included in this Report

This report summarizes FDA's performance in meeting ADUFA goals and commitments for FY 2015 and FY 2016.[2] Specifically, it updates and finalizes performance data initially reported in the FY 2015 ADUFA Performance Report and presents preliminary data on FDA's progress in meeting FY 2016 review goals, implementation activities, and accomplishments.

Review Performance

FDA continues to meet or exceed expectations in the implementation and completion of the review performance goals established under ADUFA III. Key activities and accomplishments during FY 2016 included the following:

- FDA met review-time goals for almost all (174 of 176) FY 2015 submissions that were pending at the start of FY 2016. FDA exceeded all (7 of 7) ADUFA performance goals for the FY 2015 cohort.

- Preliminary performance results indicate that FDA met review-time goals for almost all (609 of 611) FY 2016 cohort submissions reviewed and acted on as of September 30, 2016. With 216 additional reviews pending that may yet be completed on time, FDA has the potential to exceed all ADUFA performance goals for the FY 2016 cohort.

[1] www.fda.gov/forindustry/userfees/animaldruguserfeeactadufa/default.htm
[2] www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM187757.pdf and www.fda.gov/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/ucm044941.htm

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Introduction

The Animal Drug User Fee Act (ADUFA) requires the Secretary of the Department of Health and Human Services (HHS) to submit two annual reports to Congress for each fiscal year fees are collected: (1) a performance report and (2) a financial report. This report is the Food and Drug Administration's (FDA) third annual performance report to Congress under ADUFA III. Under ADUFA III, FDA agreed to meet performance goals for certain submissions over 5 years (FY 2014 through FY 2018). These review performance goals strive to improve the predictability of review time-frames of new animal drug applications (NADAs), supplemental NADAs, and investigational new animal drug (INAD) submissions. The expectation is that ADUFA will bring predictability in review times for the animal drug industry and provide FDA with resources to improve its review of applications for new animal drugs, with the result that safe and effective new products will be more readily available. The guidelines and definitions below and in Appendix A apply to the information provided in the FY 2016 report.

Information Presented in This Report

In any given year, FDA performance includes reviews of applications and submissions pending from previous fiscal years along with submissions received during the current fiscal year. This report provides FDA's final performance for the FY 2015 cohort and presents FDA's preliminary performance with respect to performance goals for the FY 2016 cohort received early enough to be reviewed, or due for review, by September 30, 2016.

The following information refers to FDA performance presented in this report.

- The term *submission* is used to refer to NADAs and reactivations, supplemental NADAs and reactivations, and INAD submissions when referencing the fiscal year cohort.

- Review-time goals are the targeted time period identified in number of calendar days in which individual submissions are to be acted on. An on-time review indicates that FDA completed action within the number of calendar days specified by the review-time goal.

- *Percent on time* refers to the percent of reviews where FDA met a review-time goal for a given type of submission. FDA's percent on time for a given type of submission is used to determine FDA's performance, and whether FDA met or exceeded the ADUFA III performance goals.

- Performance goals are the percent of total submissions, agreed to under ADUFA III, where FDA is expected to meet the review-time goal for a given type of submission. ADUFA III performance goals are established for FDA to meet the review-time goals 90 percent of the time for the defined fiscal year cohort.

- The performance statistics in this report are based on submissions received during a fiscal year, known as a receipt cohort. This methodology calculates performance statistics for submissions according to the fiscal year FDA received them, regardless of

when FDA ultimately acted on or approved the submissions. A result of this approach is that the statistics shown for a particular year may change from one report to the next. As more submissions are completed, the statistics for the year of receipt are adjusted to reflect the new completions. Therefore, until all submissions in a cohort are acted on or past the due date, whichever comes first, only a preliminary performance assessment is provided for that fiscal year cohort.

- Performance data are available on only some submissions received and acted on during FY 2016. For submission types with a longer review-time goal—for example, 180 days—early review performance data are usually limited. For those submissions with a shorter review-time goal—for example, 60 days—performance for submissions received early in the fiscal year may provide an early indicator of review performance.

- Performance goal tables indicate the total number of submissions filed as well as whether the submission was reviewed on time, was overdue, or is still pending and not past its due date. The total number of review submissions when summed together equals the total number filed.

- The workload counts presented in this report for FY 2016 includes all submissions received in the last month of FY 2016 as filed (e.g., NADA) or submitted (e.g., INAD). FDA makes a filing decision within 30 days of receiving an original application, or a proceed-to-review decision within 60 days of receiving a submission. For ADUFA review times, FDA calculates from the original receipt of the application or submission.

- Minor Use or Minor Species (MUMS) conditional approvals are not counted as NADAs. Therefore, review performance on them is not presented in this report. The goal of MUMS is to encourage development of products for treatment of minor species or for treatment of animal diseases and conditions of major species that occur infrequently or in limited geographic areas. Further details on MUMS can be found on the FDA website at: www.fda.gov/AnimalVeterinary/DevelopmentApprovalProcess/MinorUseMinorSpecies

- Submissions that FDA identified as refused to file or refused to review, and reviews that were stopped at the request of the sponsor, are not included in the statistics used to measure performance. However, these submissions are noted in the relevant workload narratives and footnotes for performance goals.

- When determining performance, FDA-calculated percentages are rounded to the nearest whole number, up to 99 percent. Percentages above 99 percent, but below 100 percent, are rounded down to 99 percent.

File Types Included in This Report

- **NADA** – An NADA is a new animal drug application including all amendments and supplements. This report presents the original application, amendments, and supplements as separate goals.
- **INAD** – Under an INAD, sponsors may submit data intended to support an application for new animal drug approval.

Source:

NADA - 21 CFR 514.3
www.ecfr.gov/cgi-bin/text-idx?SID=181eddb42cc61a7f590432800f56a462&node=se21.6.514_13&rgn=div8

INAD -
www.fda.gov/animalveterinary/guidancecomplianceenforcement/guidanceforindustry/ucm123818.htm

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ADUFA Review Workload

Review Workload: FY 2011 to FY 2016

In the table below, preliminary review workload numbers from FY 2016 are compared to the previous 5-year averages for all ADUFA application and submission types filed. There are no performance goals associated with workload, but the variations in workload over time can provide context for review performance.

As of October 1, 2014 (the beginning of FY 2015), the Agency agreed to discontinue end-review amendment (ERAs) procedures and replace them with a shorter review time process for sponsors providing electronic NADA and INAD submissions. The shortened review submissions are not a subcategory, but are now included in the overall submission numbers. The FY 2011 to FY 2015 averages include ERAs, where applicable, in order to make an accurate comparison of the change in workload.

Review Workload for Applications and Submissions

Application/ Submission Type	FY 11	FY 12	FY 13	FY 14	FY 15*	FY 16†	FY 11 to FY 15 5-Year Average	FY 16 Compared to 5-Year Average
Original NADAs and Reactivations	2	2	0	3	3	15	2	+ 650%
ERAs for Original NADAs and Reactivations	0	0	0	0	--	--		
Administrative NADAs and Reactivations	10	20	9	21	16	18	15	+ 20%
Non-manufacturing Supplemental NADAs and Reactivations	5	5	4	9	6	1	6	- 83%
ERAs for Non-manufacturing Supplemental NADAs and Reactivations	0	0	2	0	--	--		
Manufacturing Supplemental NADAs and Reactivations	378	294	281	340	327	326	324	+ 1%
Qualifying Labeling Supplements‡	--	--	--	--	3	6	--	--
INAD Studies	204	236	198	235	147	184	227	- 19%
ERAs for INAD Studies	27	19	22	45	---	---		
INAD Study Protocols	162	122	118	140	248	277	215	+ 29%
ERAs for INAD Study Protocols	81	76	55	75	--	--		

* FY 2015 numbers were changed to reflect updates to data presented in the FY 2015 ADUFA Performance Report.
† FY 2016 numbers are preliminary and will be updated in the FY 2017 ADUFA Performance Report.
‡ Qualifying Labeling Supplements were not an option under ADUFA II and the first year of ADUFA III.

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FY 2015 and FY 2016 ADUFA Performance

The tables that follow present FDA's review performance for the FY 2015 and FY 2016 ADUFA cohort submissions.

Final FY 2015 Performance

FDA exceeded the 90 percent performance level for all (7 of 7) of the review performance goals for submission types where submissions were received in FY 2015. Across all submission types, FDA met the performance goal in 748 of 750 submissions.

Application/ Submission Type	Filed	Goal: Act on 90 Percent Within	On Time	Overdue	Percent on Time
Original NADAs and Reactivations	3	180 days	3	0	100%
Administrative NADAs	16	60 days	16	0	100%
Non-manufacturing Supplemental NADAs and Reactivations	6	180 days	6	0	100%
Manufacturing Supplemental NADAs and Reactivations	327*	120 days	327	0	100%
Qualifying Labeling Supplements	3	60 days	3	0	100%
INAD Studies	147†	180 days	147	0	100%
INAD Study Protocols	248‡	60 days	246	2	99%

* A total of 351 submissions were received, but 12 received a refuse to file supplemental application and 12 received a pending supplement withdrawn by request of sponsor.
† A total of 151 submissions were received, but 2 received a file no reply with memo, 1 received a refuse to review, and 1 received a stop review.
‡ A total of 253 submissions were received, but 1 received a file no reply with memo, 2 received a refused to accept, 1 received a refuse to review, and 1 received a refuse ERA.

Preliminary FY 2016 Performance

As of September 30, 2016, performance data were available for 611 of 827 submissions filed in FY 2016. FDA is currently exceeding the review-time goal for all (7 of 7) performance goals for submission types. Overall, FDA met the performance goal in 609 of 611 submissions. With 216 submissions pending action, FDA has the potential to meet or exceed the 90 percent performance level for all (7 of 7) review performance goals.

Application/ Submission Type	Filed	Goal: Act on 90 Percent Within	On Time	Overdue	Percent On Time	Pending Within Goal	Highest Possible Percent on Time
Original NADAs and Reactivations	15*	180 days	4	0	100%	11	100%
Administrative NADAs	18	60 days	16	0	100%	2	100%
Non-manufacturing Supplemental NADAs and Reactivations	1	180 days	0	0	--	1	100%
Manufacturing Supplemental NADAs and Reactivations	326†	120 days	226	0	100%	100	100%
Qualifying Labeling Supplements	6	60 days	6	0	100%	0	100%
INAD Studies	184‡	180 days	110	0	100%	74	100%
INAD Study Protocols	277§	60 days	247	2	99%	28	99%

* A total of 16 submissions were received but 1 was voided.
† A total of 337 submissions were received, but 11 received a pending supplement withdrawn by request of sponsor.
‡ A total of 194 submissions were received, but 6 received a file no reply with memo, 3 received a refuse to review, and 1 received a stop review
§ A total of 285 submissions were received, but 2 received a file no reply with memo, 3 received a refuse to review, and 3 received a stop review.

FY 2016 Process Improvement

FDA's plans under ADUFA III (FY 2014 to FY 2018) were intended to enhance and further improve the review process via the following changes:

- **ERA.** The Agency agreed to discontinue end-review amendment procedures on October 1, 2014 (the beginning of FY 2015), and replace them with a shorter review time process for sponsors providing electronic NADA and INAD submissions.

- **Labeling Supplements.** The Agency agreed to review and act on 90 percent of qualifying labeling supplements (QLS) within 60 days after the submission date. QLS are those submitted through the use of the eSubmitter electronic submission tool, for which the sponsor provides and certifies a complete list of label changes made in the application and that the Center for Veterinary Medicine (CVM) can determine upon initial review do not decrease the safety of drug use.

- **Multiple Data Submissions to the Chemistry Manufacturing and Controls (CMC) Technical Section.** The Agency agreed to develop guidance for a two-phased CMC technical section submission and review process under the INAD file by the end of FY 2014.

- **Comparability Protocols.** The Agency will review and act on 90 percent of INAD submissions consisting of protocols without substantial data within 50 days after the submission date of the protocol. The goal is to get Agency concurrence on what data is necessary to support manufacturing changes and enable the sponsor to make manufacturing changes earlier without prior supplemental approval.

- **Manufacturing Supplemental Animal Drug Applications.** The Agency agreed to permit prior approval manufacturing supplements to be resubmitted as "Supplement-Changes Being Effected in 30 Days" (CBE-30) as described in 21 CFR 514.8(b)(3).

- **Supporting Information for Presubmission Conferences and INAD Protocols without Data Submissions.** The Agency agreed to improve the new animal drug development process to allow data which uniquely describes the general attributes of the new animal drug to be submitted earlier in the process to support more effective and efficient pre-submission conference and INAD protocol review processes.

- **Dosage Characterization.** The Agency clarified that dosage characterization is part of the effectiveness technical section of the INAD file. If information about dosage is integral to the review of a protocol, this information will be provided early to inform the review.

- **Animal Drug Availability Act (ADAA) Combinations.** The Agency agreed to explore the feasibility of pursuing statutory revisions that may modify the current requirement that the use of multiple new animal drugs in the same medicated feed be subject to an approved application.

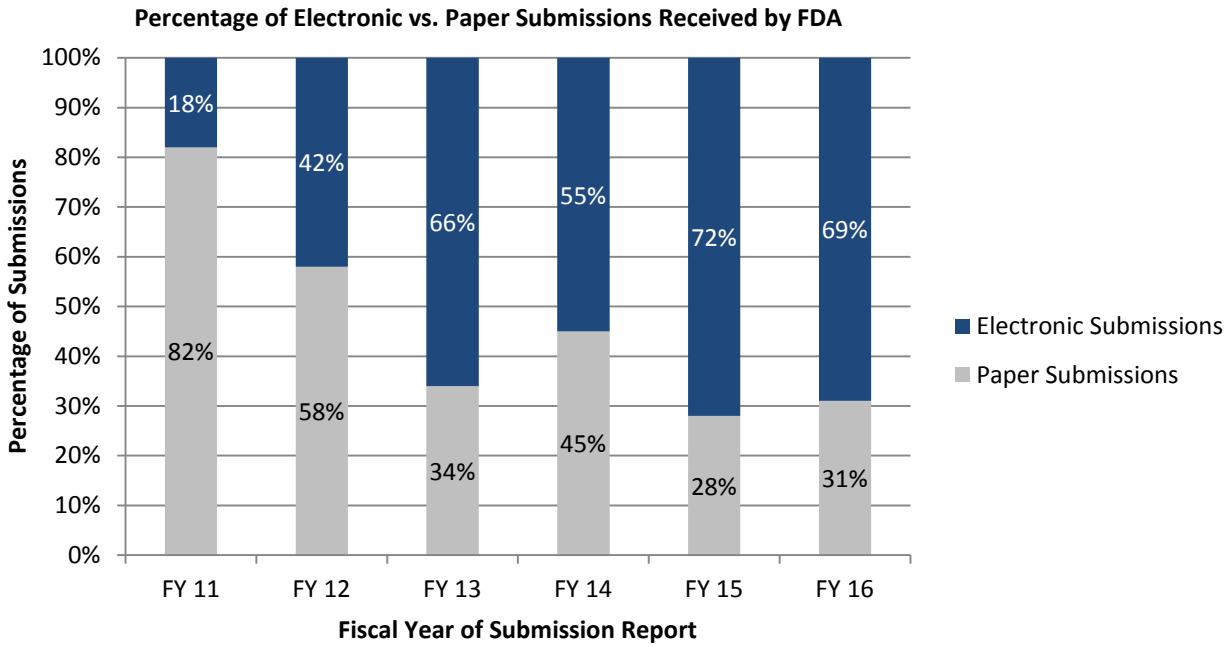
- **Conditional Approval.** The Agency agreed to explore the feasibility of pursuing statutory revisions that may expand the use of conditional approvals to other appropriate categories of new animal drug applications.

- **Microbial Food Safety Hazard Characterization Submissions.** The Agency agreed to review and act on 90 percent of microbial food safety hazard characterization submissions within 100 days after the submission date.

Major Accomplishments during FY 2016

- **Foreign Pre-approval Inspections.** In an effort to improve communications, timeliness, and predictability of foreign pre-approval inspections, sponsors can voluntarily submit a list of foreign manufacturing facilities anticipated to be included in the sponsor's new animal drug applications for the following year. Six sponsors voluntarily submitted lists of foreign manufacturing facilities anticipated to be included in new animal drug applications in FY 2016. FDA completed eight foreign pre-approval inspection assignments in FY 2016, with an average time of 86 days to complete all aspects of an inspection (e.g., preparation, communication with the foreign jurisdiction, and actual time in the facility). In comparison, FDA completed 17 foreign pre-approval inspection assignments in FY 2015 with an average time of 100 days to complete all aspects of an inspection.

- **Electronic Submission and Review.** Since the release of CVM's eSubmitter tool in FY 2011, there has been an overall decline in paper submissions. CVM received approximately 69 percent of its regulatory submissions electronically in FY 2016 (compared to 18 percent in FY 2011).



CVM's Electronic Document Submission and Review System was updated to support the ADUFA III performance goals. Specifically, eSubmitter templates were updated to accommodate the submission of manufacturing CBE-30 supplements following an incomplete prior approval manufacturing supplement, to permit the submission of comparability protocols under an INAD, to allow for the submission of two-phased CMC technical sections, to allow for the identification of Administrative NADAs, and to allow CVM to offer shortened review upon resubmission of Non-Administrative NADAs and B1

Supplements, Data Submissions, and Protocols. To support these eSubmitter changes, CVM's Appian System and Submission Tracking and Reporting System (STARS) was updated with new workflows and final action codes, respectively, to permit the efficient and timely review and completion of submissions.

- **CMC Process Enhancements**
  - **Permit a two-phase data submissions process to the CMC Technical Section:** Submission of CMC information as a two-phased data submission is voluntary. In FY 2016, CVM received no first-phase submissions according to the two-phased data submission process. This new process permits the submission and review of early completed CMC information that may increase the timely completion of the entire CMC Technical Section.
  - **Permit comparability protocols to be submitted as protocols without substantial data in an INAD file:** Submission of comparability protocols as protocols without substantial data in an INAD file is voluntary. In FY 2016, CVM received 16 INAD comparability protocols compared to 14 in FY 2015. This new process reduces the review time for most comparability protocols from 120 to 50 days.
  - **Permit prior approval manufacturing supplements to be resubmitted as CBE-30s:** In FY 2016, nine incomplete prior-approval manufacturing supplements were permitted to be resubmitted as CBE-30s. The total number of incomplete prior-approval manufacturing supplements was 28. This new process may allow for earlier distribution of animal drugs made with CMC changes.
- **Supporting Information for Presubmission Conferences and INAD Protocols without data submissions.** Early information is a collaborative process which is now used by sponsors and Office of New Animal Drug Evaluation (ONADE) reviewers to solve problems or brainstorm pathways forward in the drug development process. In FY 2016, CVM received nine early information submissions.
- **ADAA Combinations.** As reported in the FY 2015 Performance Report to Congress, the Agency held public meetings on March 16, 2015, to discuss this issue as described in the ADUFA III goals letter with stakeholders. In FY 2016, CVM fulfilled its obligation as outlined in the ADUFA III goals letter and provided written recommendations for consideration through the *Federal Register* on May 2, 2016.
- **Conditional Approval.** The conditional approval recommendations are under review.

Appendix

Appendix A: Definitions of Key Terms

Application or Supplement Withdrawn. A sponsor can notify FDA that they no longer desire to seek approval of a submitted, but pending, application or supplement. This is distinct from the Stop Review final action, because the decision is made after the NADA or supplemental application for a product is received by FDA instead of during the INAD period prior to approval. A sponsor may voluntarily request that FDA withdraw approval of an application if the sponsor represents it is no longer marketing the product. FDA also may take action to compel withdrawal of an approved application based on safety or effectiveness or certain other grounds after providing notice and an opportunity for hearing to the sponsor.

File No Reply with Memo. When FDA determines that a submission is filed without a reply to the sponsor but documentation is needed, FDA includes a review document (for example, a memorandum) in the administrative file to summarize what was included in the submission.

Refuse ERA. FDA will refuse to review an ERA submission that is determined to be insufficient on its face or otherwise of unacceptable quality upon initial inspection using criteria and procedures based on the provisions found in 21 Code of Federal Regulations (CFR) 514.110. A decision to refuse to review an ERA submission will result in the ERA being converted to a new submission of the parent submission type and the sponsor will be notified of this action.

Refuse to File Applications. Within 30 days of submission, FDA shall “refuse to file” an NADA, supplemental NADA, or reactivation determined to be inadequate or incomplete on its face or otherwise of unacceptable quality for review upon initial inspection per 21 CFR 514.110. Thus, FDA will refuse to file an application containing a large number or certain types of errors, or flaws in the development plan, that are sufficient to cause the quality of the entire submission to be questioned to such an extent that FDA cannot reasonably review it.

Refuse to Review Submissions. Within 60 days of submission, FDA will refuse to review an INAD submission determined to be insufficient on its face or otherwise of unacceptable quality upon initial inspection using criteria and procedures based on the provisions in 21 CFR 514.110. A decision to refuse to review a submission or to refuse to file an application will result in the application or submission being excluded from the cohort upon which the relevant user fee goal is based. FDA records the numbers and types of these exclusions and has included these in this annual performance report.

Review and Act on Applications and Submissions. The term "review and act on" is understood to mean the issuance of a complete action letter after the complete review of an NADA, supplemental NADA, or INAD submission that either

(1) approves an NADA or supplemental NADA or notifies a sponsor that an INAD submission is complete, or (2) sets forth in detail all of the specific deficiencies in such NADA, supplemental NADA, or INAD submission and, where appropriate, the actions necessary to place such an NADA, supplemental NADA, or INAD submission in condition for approval.

Stop Review. A sponsor may request that FDA stop the review of a particular INAD submission while the submission is under review. Any resubmission of that information is treated as a new submission, independent of previous work or data.

Department of Health and Human Services
Food and Drug Administration

This report was prepared by FDA's Office of Planning in collaboration with the Center for Veterinary Medicine (CVM). For information on obtaining additional copies contact:

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