PCoAD: The Pharmaceutical Certificate of Analysis Dataset Based on LLMs Validation and Calibration

Anonymous ACL submission

Abstract

Artificial intelligence is now widely applied in drug discovery and development, accelerating the entry of novel pharmaceuticals into clinical practice. As the variety of drugs expands, the workload for pharmaceutical inspection has increased significantly, making the demand for automated verification of pharmaceutical inspection results increasingly urgent. However, current research lacks reliable evaluation methods and datasets. To address this issue, we construct a Pharmaceutical Certificate of Analysis Dataset (PCoAD) based on large language model validation and correction. This dataset comprises 4,272 manually verified pharmaceutical certificates of analysis (PCoAs) based on Chinese and U.S. pharmacopoeias, comprehensively testing the ability of model to verify pharmaceutical inspection processes. Based on PCoAD, we propose the Multi-Agent Cooperation based on Adaptive Retrieval (MACAR) framework. This framework employs text chunking, adaptive retrieval, and inference to validate PCoAs. Experimental results demonstrate that MACAR outperforms multiple state-of-the-art methods across various types of tasks.

1 Introduction

The rapid advancement of artificial intelligence has catalyzed the transformation of the traditional pharmaceutical industry, accelerating the research and development (Zhang et al., 2025; Vora et al., 2023), production (Abraham et al., 2023; Blanco-Gonzalez et al., 2023), and clinical utilization (Xiong et al., 2023)of novel therapeutics. Consequently, an increasing number of drugs are receiving regulatory approval and entering clinical practice. While this expanding diversity of drugs enhances the quality and scope of healthcare services, it simultaneously imposes a substantially greater burden on pharmaceutical inspection systems.

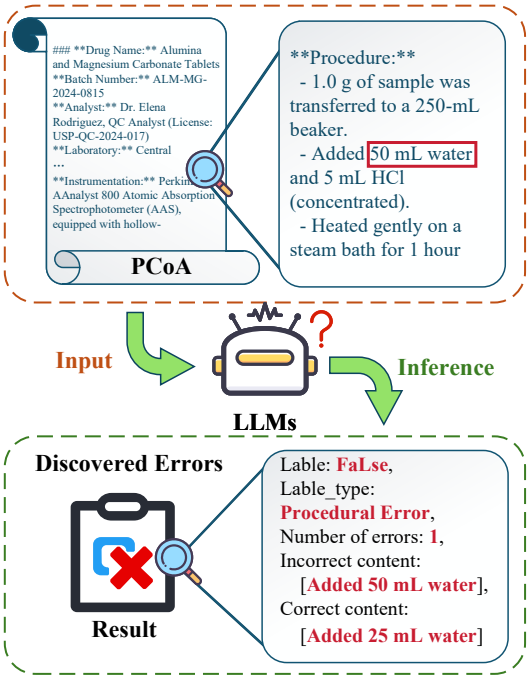


Figure 1: Task Format of PCoAD.

Pharmaceutical inspection involves complex reasoning processes such as retrieving standards, verifying inspector operational procedures, and validating computational results that demand substantial human resources(Nimmagadda, 2019). Given the immense resources required, the pharmaceutical industry increasingly urgently needs automated verification of pharmaceutical inspection processes. Large language models (LLMs), with their powerful capabilities and successful applications in the medical field (Kuang et al., 2024; Qiu et al., 2024), offer researchers a potential solution. However, current applications of LLMs in the pharmaceutical industry are primarily focused on drug discovery (Liu et al., 2024b; Tang et al., 2025), with limited exploration of automated validation within the pharmaceutical inspecting process. A key factor contributing to this gap is the absence of reliable evaluation methodologies and benchmark datasets.

To fully evaluate the capability of LLMs in the automated verification of pharmaceutical inspection processes, we conducted inferential analysis based on pharmaceutical certificates of analysis (PCoAs), which contain the items, standards and results of pharmaceutical inspection. We constructed the Pharmaceutical Certificate of Analysis Dataset (PCoAD), a dataset comprising 4,272 manually verified PCoAs. This dataset covers 792 drugs across multiple medical disciplines. To further validate LLMs' capabilities across different languages and pharmaceutical inspection standards, PCoAD incorporates both Chinese and U.S. standards. This enables comprehensive evaluation of LLMs, with the task format illustrated in Figure 1.

Since the PCoA provided by inspection institutions usually only include testing items, standards, and conclusions, rather than presenting the operational procedures, we adopted the pharmacopoeias widely used in China and the United States as the data source. We supplemented the operational procedures in PCoAs through the combined methods of LLM-based generation and manual annotation, and further constructed error datasets with corresponding validation annotations. These datasets were used to verify the capability of the model to understand pharmaceutical testing standards, analyze specific testing procedures, and calculate relevant parameters, thereby evaluating how the performs of model in the task of automated validation.

To address the challenges confronted by LLMs in the validation and correction of PCoAs, which involves long-text reasoning and information retrieval, we propose a novel framework termed Multi-Agent Cooperation based on Adaptive Retrieval (MACAR). This framework constructs three agents with distinct functionalities. The Text Chunking Agent divides the lengthy PCoAs text into independent sub-sections to reduce contextual length during retrieval and reasoning. The Adaptive Retrieval Agent analyzes missing knowledge, iteratively retrieves nested content. The Inference Agent then performs localized reasoning on each subsection alongside retrieved evidence, with the capability to re-invoke the retrieval agent mid-inference for dynamic information supplementation. Finally, all results are merged to enable detailed argumentation and verification of the PCoAs.

Extensive experiments demonstrate that MACAR outperforms baseline models, achieving an average improvement of 3.27% over the strongest baseline. Our results underscore the potential of this novel task and dataset to advance future research in the field.

The main contributions of this paper are as follows:

(1) We introduce and formalize the LLM-based task of verifying and rectifying PCoAs, a novel text validation task involving long-text reasoning and information retrieval, which provides an evaluation paradigm for the automated inspection of pharmaceutical inspecting processes;

(2) We construct the PCoAD, a novel benchmark dataset where PCoAs are constructed via a dual paradigm of LLM-driven generation and expert manual annotation. The PCoAD enables a comprehensive evaluation of the efficacy of models in automating the verification workflows of pharmaceutical inspecting processes;

(3) We develop a method named as Multi-Agent Cooperation based on Adaptive Retrieval (MACAR) as a baseline method.

2 Related work

2.1 Artificial intelligence in drug industry

The development of LLMs technologies, has profoundly transformed the pharmaceutical industry. The capabilities of LLMs have been extensively explored and applied across drug development stages. Context learning reduces the data demand for drug molecule discovery (Li et al., 2024a); LLMs robust capacity to encode chemical reaction pathways provides feasible synthetic routes for drug development (Wang et al., 2025; Bakkar et al., 2018); Inherent knowledge base enables effective analysis of pharmacological properties (Das and Chakraborty, 2026; Shin et al., 2024); Moreover, the development of protein models by integrating the emergent abilities of LLMs has emerged as a prominent research hotspot (Xiao et al., 2024b; Fan et al., 2025). Beyond leveraging existing LLM capabilities for drug development, another major research direction involves constructing benchmarks to explore LLMs' potential in the pharmaceutical domain, covering areas such as drug-target interaction (Arevalo et al., 2024), drug-induced toxicity (Silberg et al., 2024), and small molecule drug discovery (Liu et al., 2024c). Although these efforts have accelerated drug discovery, they have overlooked the potential of LLMs in drug testing applications that require significant human cost.

2.2 Text Error Correction Based on Large Models

The powerful capabilities of LLMs have enabled them to achieve promising results in traditional text semantic error correction. C-LLM (Li et al., 2024b) leverages character-level tokenization to improve the performance of spelling checking. Tom Potte et al rely on the multilingual generalization ability of LLMs to realize grammatical error correction(Potter and Yuan, 2024). Although these methods effectively address semantic errors in text, they are unable to handle logical and factual errors efficiently.

To overcome this limitation, one strategy introduces external knowledge sources, such as Wikipedia (Zakka et al., 2024) and knowledge graphs (Jiang et al., 2023), to comprehensively correct errors in text through Retrieval-Augmented Generation (RAG). Building on this, researchers have further incorporated modules such as reranking modules (Kim et al., 2024) and readers (Fang et al., 2024) to enhance performance. To avoid introducing noise during retrieval, adaptive retrieval can be achieved by constructing triples (Fang et al., 2025), analyzing self-attention weights (Su et al., 2024), and system state variables (Jiang et al., 2025). Nevertheless, high-quality external knowledge is difficult to obtain. Thus, another approach utilizes the inherent capabilities of LLMs themselves to enable autonomous text error correction through multi-model interaction methods. Among these approaches, constructing frameworks that mimic human behaviors, such as reflection (Shinn et al., 2023), debate (Liang et al., 2024; Liu et al., 2025), and discussion (Lingam et al., 2025), has become a major research direction. However, the average length of datasets for text error correction is relatively short, and the effectiveness of RAG-based and multi-model interaction-based methods in long-text correction remains understudied.

3 Pharmaceutical Certificate of Analysis Dataset

PCoAD comprises 4,272 PCoAs spanning 20 medical specialties and 792 distinct drugs. For erroneous PCoAs, extensive annotations across multiple validation dimensions are provided. To clarify the utility of this dataset, the dataset construction and annotation processes are detailed below (see Figure 2). The objectives of the PCoAD are as follows: (1) retrieving all relevant Monographs and General Chapters for a given PCoA; and (2) evaluating whether the PCoA complies with these standards. Where discrepancies are identified, the system is required to specify the error type, number of errors, and exact error content, and propose appropriate corrective actions. Detailed prompts for implementing these objectives and annotating errors are provided in Appendix A.1.

3.1 Dataset Preparation

To construct PCoAD, the Pharmacopoeia of the People's Republic of China (ChP 2020) and the United States Pharmacopeia (USP 2023) were adopted as foundational documents. For drug selection from these pharmacopoeias, a hybrid strategy integrating search popularity metrics and random sampling was employed, which is designed to ensure the representativeness and diversity of the constructed dataset.

A key challenge in PCoAD data extraction lies in constructing detailed and comprehensive inspection items for each drug. This challenge arises because pharmacopoeias are structured into monographs (focused on specific pharmaceutical inspection) and general chapters, with a cross-referenced graph structure between these two components—an arrangement that impedes the acquisition of detailed inspection items. To address this obstacle, identifiers were first extracted from both monographs and general chapters via regular expressions. Breadth-first search was then employed to retrieve the general chapters required for each monograph, with subsequent removal of duplicate entries and content irrelevant to pharmaceutical inspection.

A subsequent challenge is that certain content in general chapters is only applicable to specific scenarios; indiscriminate extraction of such content would introduce irrelevant inspection items. To address this, the monograph and its corresponding general chapter are fed into LLMs, which are leveraged to distinguish scenario-specific content and extract only the required inspection items. Finally, manual error correction is performed to refine the results, yielding the complete set of inspection items I_n.

3.2 Data Generation

Notably, the PCoAs currently issued by government authorities generally lack documented operating procedures. To fully verify the capability of LLMs in the automated verification of phar-

maceutical inspection, detailed operational steps were supplemented to these PCoAs. To further enhance PCoA diversity, four distinct roles were designed: Meticulous New Employee, Careless New Employee, Rigorous Expert, and Fatigued Expert. These roles were then utilized to generate PCoAs with detailed experimental procedures based on the I_n, where the generated PCoAs reflect the characteristics of each role. Subsequent manual verification yielded validated PCoAs; to ensure the consistency of drug types and proportions, at least one valid PCoA was retained for each drug. The final dataset was designated as P_{COA}.

3.3 Labeling Errors

Based on the textual characteristics of P_{COA}, four common error types were first defined, as follows: (1) Standard Error: A P_{COA} cites an incorrect standard; (2) Procedure Error: The experimental operations described in a P_{COA} are defective; (3) Step Omission: A P_{COA} lacks specific inspection items as specified in the complete inspection item set I_n; (4) Calculation Error: The calculation results presented in a P_{COA} are inaccurate. Beyond these common types, PCoAD incorporates a unique error type, logic errors induced by LLM hallucinations, that distinguishes it from other datasets in the pharmaceutical industry. Specifically, a logic error occurs when the result of a specific inspection step in a P_{COA} is revised through flawed reasoning in subsequent text, ultimately leading to an incorrect conclusion. This unique error type is designed to evaluate model ability to resist hallucinations during the automated verification of pharmaceutical inspection processes.

For the four common error types, 1–4 modifications were introduced to P_{COA} content using LLMs, with corresponding error information annotated. Regarding logic error data, these were primarily obtained via manual screening of erroneous P_{COA} generated by LLMs. Owing to their autonomous generation by LLMs and origin in hallucinations, such data exhibit high deceptiveness to models. Furthermore, existing studies have demonstrated that flawed reasoning logic can trigger hallucinations in LLMs (Ji et al., 2023). Accordingly, logic error data were required to incorporate erroneous reasoning processes that alter the core conclusions of P_{COA}. Notably, logic errors are designed to simulate malicious tampering by operators in real-world scenarios, thereby testing model reliability when faced with such tampering behaviors. By constructing data covering these five error types, a reliable dataset was established to enable comprehensive evaluation of model performance in the automated verification of pharmaceutical inspection processes.

Statistics	ChP(2020)	USP (2023)
True	1,083	1,053
Standard Error	201	208
Procedural Error	242	206
Step Omission	230	212
Calculation Error	202	203
Logical Error	208	224
Avg len	6,279.18	4,870.62
Avg input len	43,242.65	55,082.67

Table 1: Statistical information for PCoAD. Avg len represents the average number of tokens in PCoAs; Avg input len represents the average number of tokens for PCoAs and required knowledge.

3.4 Statistical Analysis

Statistical information for PCoAD is presented in Table 1, which indicates that the average input length of PCoAD exceeds that of other long-text tasks (e.g., the average length in LongBench (Bai et al., 2025) does not exceed 30,000 tokens). Prior work has demonstrated that as input token count increases, LLMs experience gradual performance degradation, a phenomenon termed "context rot" (Hong et al., 2025; Liu et al., 2024a), and may even exhibit critical failure in task execution. Consequently, the excessively long input contexts of PCoAD constitute a prominent challenge for automated pharmaceutical inspection verification models.

4 Methodology

In this section, we propose the Multi-Agent Cooperation based on Adaptive Retrieval (MACAR) framework, a novel agent framework designed to address the challenges of PCoAD, as shown in Figure 2. Agent prompts are shown in Appendix B.

4.1 Text Chunking Agent

To mitigate the challenge of excessively long contexts in PCoAD and prevent context rot during inference, a Text Chunking Agent is introduced, which reduces input length by partitioning PCoAs into semantically coherent segments. The agent first extracts salient keywords, typically drug

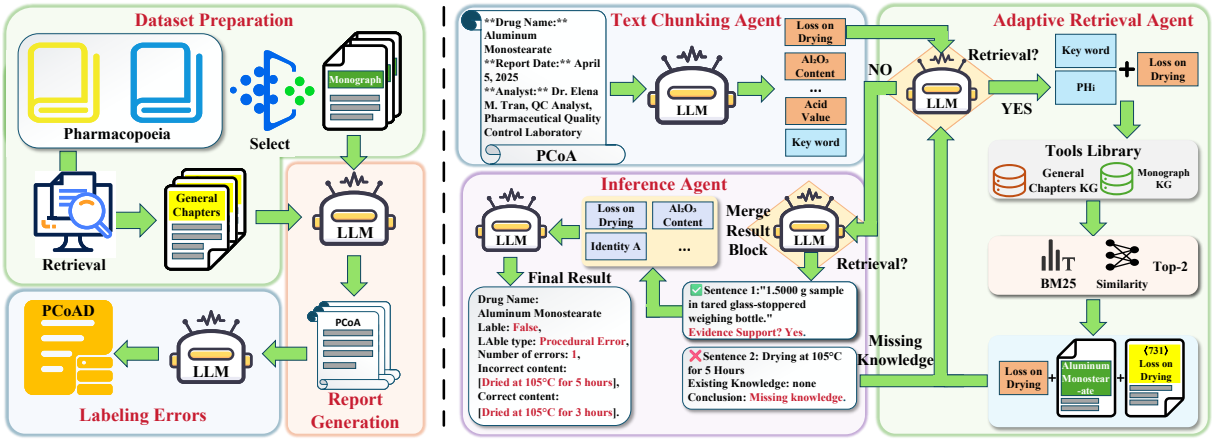


Figure 2: PCoAD construction workflow (left) and Overall framework of MACAR (right).

names, from the PCoA to serve as anchors, minimizing the inclusion of irrelevant content. The PCoA is then segmented by inspection item, a strategy aligned with the structure of pharmaceutical standards, where each inspection item corresponds to a specific requirement in a Monograph or General Chapter. This inspection item-based segmentation not only enhances retrieval precision by aligning with the normative structure of pharmacopoeias but also significantly shortens the context length per inference unit. Each resulting segment is concatenated with its associated anchor keyword and passed to the Adaptive Retrieval Agent for subsequent verification-related processing.

4.2 Adaptive Retrieval Agent

The nested reference structure of pharmaceutical inspection standards presents challenges for retrieval. To address this issue, an Adaptive Retrieval Agent is proposed, which employs an adaptive mechanism to target the complexities of nested references. First, the agent determines whether each input segments requires retrieval of pharmaceutical standard content. For segments that do not rely on external pharmaceutical standard knowledge, such as pharmaceutical production information and personnel details, the retrieval process can be entirely skipped, thereby minimizing the introduction of irrelevant noise.

For segments requiring retrieval, the Adaptive Retrieval Agent first selects an appropriate knowledge base and generates a targeted retrieval phrase PH_i. A hybrid retrieval strategy is then applied by combining the segment, extracted keywords, and PH_i. We employ BM25 (Robertson and Walker, 1994) for sparse retrieval, calculated, yielding retrieval $Score_1$, and complement it with dense retrieval based on semantic similarity, producing a $Score_2$. Finally, the two scores are weighted differently and added to yield the final retrieval score. The calculation formula is as follows.

$$\text{Score}_1(D, PH_i) = \sum_{i=1}^{n} \text{IDF}(w_i) \times \frac{f(ph_i, D)(k_1 + 1)}{f(ph_i, D) + k_1 \left(1 - b + b\frac{|D|}{\text{avgdl}}\right)} \quad (1)$$

$$\text{IDF}(w_i) = \log\left(\frac{N_D - \text{num}(\text{ph}_i) + 0.5}{\text{num}(\text{ph}_i) + 0.5} + 1\right) \quad (2)$$

$$\text{Score}_2(D, W) = \frac{E(D)^T E(W)}{\|E(D)\|\|E(W)\|} \quad (3)$$

$$\text{Score}_{ij} = \alpha \text{Score}_1 + (1 - \alpha)\text{Score}_2 \quad (4)$$

D represents a document in the knowledge base, avgdl denotes the average length of all documents, $\{ph\}_i$ is the i-th word in the search phrase, $f(\{ph\}_i, D)$ is the frequency of $\{ph\}_i$ in document D, num(ph_i) denotes the number of documents containing ph_i, and N_D denotes the total number of documents in the document collection, $|D|$ is the length of document D, and $E(D)$ is the vectorization of D. k_1, b, α are hyperparameters.

Given the high specialization of pharmaceutical inspection standards and differences between

various drugs, only the top two highest-scoring relevant knowledge segments are retrieved for each segment in the process, this constraint helps avoid information overload and ensures the relevance of retrieved content. Subsequently, the Adaptive Retrieval Agent reassesses whether the acquired knowledge is sufficient to support reasoning about the input sub-part. If the reasoning requirement is satisfied, the retrieval process is concluded; otherwise, the retrieval-reassessment cycle is repeated until the reasoning requirement is met or the maximum retrieval count Z is reached.

4.3 Inference Agent

For the Inference Agent, each sub-section undergoes a separate inference process first. During this process, to acquire sufficient relevant knowledge, if the Inference Agent determines that necessary information is lacking for inference, it will resubmit that sub-section to the Adaptive Retrieval Agent for renewed retrieval. For efficiency considerations, the Inference Agent is permitted only one re-retrieval attempt per sub-section. Finally, after completing inference for all subcomponents, the inference agent synthesizes all inference results to generate the final answer, concluding the verification process.

5 Experiment

5.1 Experimental Setup

Evaluation Metrics. We define five evaluation dimensions, where RA denotes Report Authenticity, EC denotes Error Classification, NE denotes Number of Errors, IC denotes Incorrect Content, and RC denotes Rectified Content. For RA, EC, and NE, we adopt accuracy as the evaluation metric. For IC and RC, there may be 0 to 4 possible outputs. Referring to previous studies (Feng et al., 2024), we adopt the F1-score of the multi-label text classification task. The specific calculation method is shown in Equation 5.

$$F1 = \frac{1}{N}\sum_{i=1}^{N}\frac{2\left|y^{(i)} \cap \hat{y}^{(i)}\right|}{\left|y^{(i)}\right| + \left|\hat{y}^{(i)}\right|} \tag{5}$$

$y^{(i)}$ denotes the true label of the i-th sample, while $\hat{y}^{(i)}$ represents the predicted label of the i-th sample. In this paper, since both the incorrect content and rectified content are expressed in natural language, we define that two pieces of content are considered identical when the semantic similarity between the generated content and the labeled content is no less than 0.95. Take the average of three experimental results.

Baselines. To evaluate the effectiveness of MACAR, we compared it with 10 baselines. (1)Advanced RAG: CoK(Li et al., 2024c), SuRe(Kim et al., 2024) and HyKGE(Jiang et al., 2023); (2) Adaptive RAG: Self-RAG(Asai et al., 2024), DRAGIN(Su et al., 2024), KiRAG(Fang et al., 2025) and TC–RAG(Jiang et al., 2025); (3)Agent: MAD(Liang et al., 2024), DoT(Lingam et al., 2025), DMAD(Liu et al., 2025). Further details are provided in Appendix C.1.

Implementation details. In practical scenarios, PCoAs are subject to stringent confidentiality and data privacy requirements, rendering the direct use of commercial LLM APIs unsuitable due to security concerns. To balance model performance with the need for local deployment, we adopt the open-source Qwen3-14B(Yang et al., 2025) as our base model and bge-large-en-v1.5 (Xiao et al., 2024a) as the encoder. The hyperparameters in MACAR are set as follows: k_1=1.5, b=0.75, α=0.6, and a maximum retrieval count Z=5. To enhance response diversity, the temperature is set to 0.5. Further details are provided in Appendix C.2.

5.2 Main results

Table 2 presents the experimental results of the baseline and MACAR on PCoAD, where MACAR significantly outperforms the baseline. Compared to Advanced RAG, MACAR achieves adaptive retrieval, enabling precise knowledge acquisition while reducing noise, thereby delivering substantial improvements. In contrast, Adaptive RAG suffers from context rot during reasoning due to excessive retrieved information. MACAR avoids this issue by constructing a Text Chunking Agent. Additionally, comparing agents reveals that knowledge solely from LLMs struggles to address specialized challenges in PCoAD. However, model interactions enhance the assessment of PCoA authenticity. MACAR effectively resolves issues present in the baseline, achieving an average 3.27% improvement over the best baseline method (TC–RAG).

Meanwhile, we also observed that MACAR and the baseline model exhibit similar performance on both IC and RI metrics. This indicates that once a model can accurately identify erroneous content, it can effectively correct errors through relevant knowledge and self-reasoning, further demonstrating the application potential of LLMs in pharma-

Type	Method	ChP(2020)					USP(2023)				
		RA ACC	EC ACC	NE ACC	IC F1	RC F1	RA ACC	EC ACC	NE ACC	IC F1	RC F1
Advanced RAG	CoK	53.28	45.54	50.15	48.18	47.68	56.39	47.95	54.93	51.06	50.44
	SuRe	54.77	46.27	51.31	50.12	49.45	58.98	49.89	57.70	53.61	50.74
	HyKGE	57.32	48.37	52.74	51.51	51.06	59.95	50.75	58.96	54.93	54.16
Adaptive RAG	Self-RAG	57.15	48.74	53.41	52.08	51.69	60.25	50.79	59.26	54.86	54.25
	DRAGIN	59.49	49.21	53.78	52.23	51.41	61.22	51.29	59.88	54.35	54.53
	KiRAG	60.11	50.51	55.92	55.02	54.37	63.24	56.59	62.72	58.39	56.50
	TC-RAG	60.46	51.35	56.16	54.86	53.46	63.33	**53.72**	62.64	57.87	57.17
Agent	MAD	58.16	46.62	50.97	48.69	47.48	56.78	50.66	61.28	50.84	49.36
	DoT	60.84	49.28	53.23	51.20	50.68	61.81	53.27	63.06	54.89	53.66
	DMAD	61.56	48.65	53.39	50.56	49.68	61.98	52.68	63.15	54.61	54.15
Ours	MACAR	**62.34**	**52.12**	**60.54**	**56.48**	**55.86**	**65.36**	53.49	**63.85**	**60.15**	**59.56**

Table 2: Experimental results of MACAR and baseline on PCoAD. The best scores are displayed in bold, while the second-best results are underlined.

Method	ChP(2020)					USP(2023)				
	RA	EC	NE	IC	RC	RA	EC	NE	IC	RC
MACAR w/o T	60.28	51.59	56.74	55.02	54.22	64.06	52.59	63.10	58.29	57.42
MACAR w/o R	58.29	49.64	54.15	53.35	52.91	62.57	51.36	58.56	56.49	56.03
MACAR w/o I	61.61	51.87	56.08	54.59	53.94	63.14	53.03	54.93	57.08	56.37

Table 3: Ablation experiment results.

ceutical verification. When comparing different pharmacopoeias, MACAR and the baseline model achieved better performance on USP (2023). This may be attributed to USP (2023) having a lower nesting complexity than ChP (2020), coupled with its widespread real-world adoption. Consequently, portions of its content were likely incorporated into the pre-training corpus and learned by LLMs.

5.3 Ablation Studies

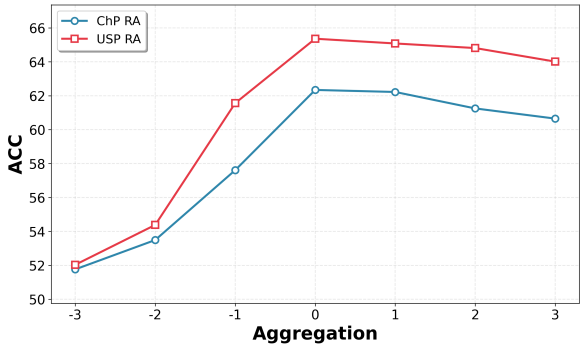
As shown in Table 3, we weakened MACAR in three aspects: (1) w/o T disabled the text segmentation agent, feeding the entire PCoA directly into subsequent modules; (2) w/o R disabled the adaptive retrieval agent; and (3) w/o I merged all subparts and generated the answer directly. When the text segmentation agent is absent, MACAR performs similarly to Adaptive RAG, relying solely on the reasoning agent to acquire additional information. Disabling the adaptive retrieval agent caused MACAR's performance to drop significantly due to the loss of external knowledge. However, the text segmentation agent still reduced the context required per inference, resulting in overall superiority over DMAD. Finally, disabling the reasoning agent allowed the additional retrieval information from text segmentation to help the model maintain its judgment on PCoA correctness. Yet, the increased information led to context decay, causing a decline in error identification capability.

5.4 Influence of Text Chunking Granularity

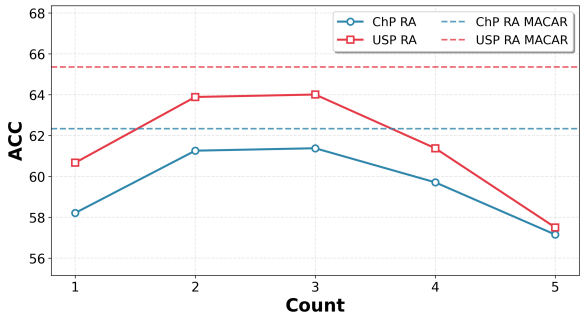
We further aggregated and subdivided the chunking results from the Text Chunking Agent to observe their impact on MACAR performance. The experimental results are shown in Figure 3a. Where, a positive aggregation count indicates that two adjacent text chunks underwent one aggregation operation. A negative aggregation count signifies that the original text chunk was subjected to another subdivision operation. Figure 3a reveals that chunking by inspection items yields the optimal strategy. Increasing chunk size elongates the context input to the inference agent, degrading model performance. Conversely, finer-grained text chunking increases retrieval difficulty. Since some content overlaps across different monographs, excessive text fragmentation prevents the model from correctly acquiring knowledge. Moreover, too many blocks increase the context length during the inference agent's final summarization. The combined effect of these factors causes rapid model performance degradation. Therefore, a reasonable chunk size contributes to improved model performance.

Method	ChP(2020)				USP(2023)			
	RA		NE		RA		NE	
	FP	FN	FP	FN	FP	FN	FP	FN
MACAR	36.52%	63.48%	23.70%	76.30%	31.22%	68.78%	29.31%	70.69%
TC-RAG	87.23%	12.77%	86.27%	13.73%	85.36%	14.64%	89.59%	10.41%
DMAD	28.21%	71.79%	31.38%	68.62%	23.74%	76.26%	38.64%	61.36%

Table 4: Relative proportions of various error types in baseline and MACAR relative to total errors.



(a) The impact of text chunking granularity on MACAR performance.



(b) The impact of iteration count in retrieval on MACAR performance.

Figure 3: The influence of parameters.

5.5 Influence of Iteration Count in Retrieval

We imposed a constraint on the number of retrieval iterations for the MACAR and simultaneously examined the mechanism by which retrieval rounds and retrieval quantities influence overall performance. As shown in Figure 3b, when the retrieval count is limited to 1, MACAR fails to address the nested evaluation criteria issue in PCoAD. Conversely, excessive retrieval introduces significant noise, compounded by context rot, causing rapid model performance degradation. Simultaneously, we observe that rigidly enforcing retrieval limits restricts model flexibility. Such as, when processing query fragments related to product information, unnecessary information is still retrieved, introducing irrelevant context and further degrading overall performance. Therefore, MACAR's adaptive retrieval strategy enhances retrieval precision and improves model performance.

5.6 Error Analysis

Statistical analysis of error data from the baseline and MACAR models on the PCoAD dataset is summarized in Table 4. For NE tasks, FP indicates predictions below actual values, and FN indicates predictions exceeding actual values. In authenticity assessment, RAG-based methods were more inclined to classify PCoAD as TRUE, a bias caused by the models' over-acquisition of pharmaceutical inspection standards, which induces contextual rot during final judgment. Conversely, the agent-based approach showed the opposite trend, likely due to excessive deliberation in its multi-model debate framework. Regarding NE, the baseline and MACAR also exhibited significant discrepancies. RAG-based errors mainly caused by incomplete statistics that models halted reasoning upon detecting the first text error, without scanning the full report. In contrast, MACAR and agent-based methods exhibited reverse behavior, driven by their block-based. This occurs because when errors occur during reasoning, they propagate to the integration stage, thereby increasing the total error count.

6 Conclusion

We propose a task for validating PCoA and construct a dataset (PCoAD) covering both Chinese and American standards to further support this task. We also introduce MACAR, a novel agent framework based on adaptive retrieval that can segment long texts and perform retrieval and reasoning independently. Our experimental results demonstrate that MACAR outperforms state-of-the-art RAG and agent-based methods. Due to the complexity of PCoAD, model performance still holds room for improvement. Enhancing the effective identification and judgment of error types and error descriptions represents a future research direction.

Limitations

Despite the contributions of this work, several limitations must be acknowledged and addressed in future research. First, in PCoAD, although we designed varying error counts, the proportion of error counts was imbalanced after manual screening, potentially undermining the model's ability to effectively identify error counts. Furthermore, although PCoAD underwent multiple rounds of manual verification, the inherent specialization and complexity of PCoA and pharmacopoeia data inevitably introduced some invalid entries, potentially influencing experimental outcomes. The multi-agent interaction process within MACAR failed to fully leverage all models, indicating room for further optimization.

References

John Abraham and 1 others. 2023. *Science, politics and the pharmaceutical industry: Controversy and bias in drug regulation*. Routledge.

John Arevalo, Ellen Su, Anne E Carpenter, and Shantanu Singh. 2024. Motive: A drug-target interaction graph for inductive link prediction. *Advances in Neural Information Processing Systems*, 37:140320–140333.

Akari Asai, Zeqiu Wu, Yizhong Wang, Avirup Sil, and Hannaneh Hajishirzi. 2024. Self-RAG: Learning to retrieve, generate, and critique through self-reflection. In *The Twelfth International Conference on Learning Representations*.

Yushi Bai, Shangqing Tu, Jiajie Zhang, Hao Peng, Xiaozhi Wang, Xin Lv, Shulin Cao, Jiazheng Xu, Lei Hou, Yuxiao Dong, and 1 others. 2025. Longbench v2: Towards deeper understanding and reasoning on realistic long-context multitasks. In *Proceedings of the 63rd Annual Meeting of the Association for Computational Linguistics (Volume 1: Long Papers)*, pages 3639–3664.

Nadine Bakkar, Tina Kovalik, Ileana Lorenzini, Scott Spangler, Alix Lacoste, Kyle Sponaugle, Philip Ferrante, Elenee Argentinis, Rita Sattler, and Robert Bowser. 2018. Artificial intelligence in neurodegenerative disease research: use of ibm watson to identify additional rna-binding proteins altered in amyotrophic lateral sclerosis. *Acta neuropathologica*, 135(2):227–247.

Alexandre Blanco-Gonzalez, Alfonso Cabezon, Alejandro Seco-Gonzalez, Daniel Conde-Torres, Paula Antelo-Riveiro, Angel Pineiro, and Rebeca Garcia-Fandino. 2023. The role of ai in drug discovery: challenges, opportunities, and strategies. *Pharmaceuticals*, 16(6):891.

Debojyoti Das and Debdutta Chakraborty. 2026. In-silico identification of a doxorubicin alternative with reduced cardiotoxicity informed by llm-assisted modeling. *Journal of Molecular Graphics and Modelling*, 142:109217.

Wenqi Fan, Yi Zhou, Shijie Wang, Yuyao Yan, Hui Liu, Qian Zhao, Le Song, and Qing Li. 2025. Computational protein science in the era of large language models (llms). *arXiv preprint arXiv:2501.10282*.

Feiteng Fang, Yuelin Bai, Shiwen Ni, Min Yang, Xiaojun Chen, and Ruifeng Xu. 2024. Enhancing noise robustness of retrieval-augmented language models with adaptive adversarial training. In *Proceedings of the 62nd Annual Meeting of the Association for Computational Linguistics (Volume 1: Long Papers)*, pages 10028–10039.

Jinyuan Fang, Zaiqiao Meng, and Craig MacDonald. 2025. KiRAG: Knowledge-driven iterative retriever for enhancing retrieval-augmented generation. In *Proceedings of the 63rd Annual Meeting of the Association for Computational Linguistics (Volume 1: Long Papers)*, pages 18969–18985, Vienna, Austria. Association for Computational Linguistics.

Jianzhou Feng, Lazhi Zhao, Haonan Qin, Yiming Xu, and Ziqi Wang. 2024. Cadlra: A multi-charge prediction method based on the criminal act-driven law retrieval augmentation. *Engineering Applications of Artificial Intelligence*, 134:108619.

Kelly Hong, Anton Troynikov, and Jeff Huber. 2025. Context rot: How increasing input tokens impacts llm performance. Technical report, Chroma.

Ziwei Ji, Nayeon Lee, Rita Frieske, Tiezheng Yu, Dan Su, Yan Xu, Etsuko Ishii, Ye Jin Bang, Andrea Madotto, and Pascale Fung. 2023. Survey of hallucination in natural language generation. *ACM computing surveys*, 55(12):1–38.

Xinke Jiang, Yue Fang, Rihong Qiu, Haoyu Zhang, Yongxin Xu, Hao Chen, Wentao Zhang, Ruizhe Zhang, Yuchen Fang, Xinyu Ma, and 1 others. 2025. Tc–rag: Turing–complete rag's case study on medical llm systems. In *Proceedings of the 63rd Annual Meeting of the Association for Computational Linguistics (Volume 1: Long Papers)*, pages 11400–11426.

Xinke Jiang, Ruizhe Zhang, Yongxin Xu, Rihong Qiu, Yue Fang, Zhiyuan Wang, Jinyi Tang, Hongxin Ding, Xu Chu, Junfeng Zhao, and 1 others. 2023. Hykge: A hypothesis knowledge graph enhanced framework for accurate and reliable medical llms responses. *arXiv preprint arXiv:2312.15883*.

Jaehyung Kim, Jaehyun Nam, Sangwoo Mo, Jongjin Park, Sang-Woo Lee, Minjoon Seo, Jung-Woo Ha, and Jinwoo Shin. 2024. Sure: Summarizing retrievals using answer candidates for open-domain QA of LLMs. In *The Twelfth International Conference on Learning Representations*.

Keying Kuang, Frances Dean, Jack B Jedlicki, David Ouyang, Anthony Philippakis, David Sontag, and Ahmed M Alaa. 2024. Med-real2sim: Non-invasive medical digital twins using physics-informed self-supervised learning. *Advances in Neural Information Processing Systems*, 37:5757–5788.

Jiatong Li, Yunqing Liu, Wenqi Fan, Xiao-Yong Wei, Hui Liu, Jiliang Tang, and Qing Li. 2024a. Empowering molecule discovery for molecule-caption translation with large language models: A chatgpt perspective. *IEEE transactions on knowledge and data engineering*, 36(11):6071–6083.

Kunting Li, Yong Hu, Liang He, Fandong Meng, and Jie Zhou. 2024b. C-llm: Learn to check chinese spelling errors character by character. In *Proceedings of the 2024 Conference on Empirical Methods in Natural Language Processing*, pages 5944–5957.

Xingxuan Li, Ruochen Zhao, Yew Ken Chia, Bosheng Ding, Shafiq Joty, Soujanya Poria, and Lidong Bing. 2024c. Chain-of-knowledge: Grounding large language models via dynamic knowledge adapting over heterogeneous sources. In *The Twelfth International Conference on Learning Representations*.

Tian Liang, Zhiwei He, Wenxiang Jiao, Xing Wang, Yan Wang, Rui Wang, Yujiu Yang, Shuming Shi, and Zhaopeng Tu. 2024. Encouraging divergent thinking in large language models through multi-agent debate. In *Proceedings of the 2024 conference on empirical methods in natural language processing*, pages 17889–17904.

Vijay Lingam, Behrooz Omidvar Tehrani, Sujay Sanghavi, Gaurav Gupta, Sayan Ghosh, Linbo Liu, Jun Huan, and Anoop Deoras. 2025. Enhancing language model agents using diversity of thoughts. In *The Thirteenth International Conference on Learning Representations*.

Nelson F Liu, Kevin Lin, John Hewitt, Ashwin Paranjape, Michele Bevilacqua, Fabio Petroni, and Percy Liang. 2024a. Lost in the middle: How language models use long contexts. *Transactions of the Association for Computational Linguistics*, 12:157–173.

Sizhe Liu, Yizhou Lu, Siyu Chen, Xiyang Hu, Jieyu Zhao, Yingzhou Lu, and Yue Zhao. 2024b. Drugagent: Automating ai-aided drug discovery programming through llm multi-agent collaboration. *arXiv preprint arXiv:2411.15692*.

Yexiang Liu, Jie Cao, Zekun Li, Ran He, and Tieniu Tan. 2025. Breaking mental set to improve reasoning through diverse multi-agent debate. In *The Thirteenth International Conference on Learning Representations*.

Yunchao Liu, Ha Dong, Xin Wang, Rocco Moretti, Yu Wang, Zhaoqian Su, Jiawei Gu, Bobby Bodenheimer, Charles Weaver, Jens Meiler, and 1 others. 2024c. Welqrate: Defining the gold standard in small molecule drug discovery benchmarking. *Advances in Neural Information Processing Systems*, 37:53222–53236.

Venkata Siva Prakash Nimmagadda. 2019. Explainable ai in regulatory compliance for pharmaceutical manufacturing. *European Journal of Quantum Computing and Intelligent Agents*, 3:341–382.

Tom Potter and Zheng Yuan. 2024. Llm-based code-switched text generation for grammatical error correction. In *Proceedings of the 2024 Conference on Empirical Methods in Natural Language Processing*, pages 16957–16965.

Pengcheng Qiu, Chaoyi Wu, Xiaoman Zhang, Weixiong Lin, Haicheng Wang, Ya Zhang, Yanfeng Wang, and Weidi Xie. 2024. Towards building multilingual language model for medicine. *Nature Communications*, 15(1):8384.

Stephen E Robertson and Steve Walker. 1994. Some simple effective approximations to the 2-poisson model for probabilistic weighted retrieval. In *SIGIR'94: Proceedings of the Seventeenth Annual International ACM-SIGIR Conference on Research and Development in Information Retrieval, organised by Dublin City University*, pages 232–241. Springer.

Euibeom Shin, Yifan Yu, Robert R Bies, and Murali Ramanathan. 2024. Evaluation of chatgpt and gemini large language models for pharmacometrics with nonmem. *Journal of Pharmacokinetics and Pharmacodynamics*, 51(3):187–197.

Noah Shinn, Federico Cassano, Ashwin Gopinath, Karthik Narasimhan, and Shunyu Yao. 2023. Reflexion: Language agents with verbal reinforcement learning. *Advances in Neural Information Processing Systems*, 36:8634–8652.

Jacob Silberg, Kyle Swanson, Elana Simon, Angela Zhang, Zaniar Ghazizadeh, Scott Ogden, Hisham Hamadeh, and James Y Zou. 2024. Unitox: leveraging llms to curate a unified dataset of drug-induced toxicity from fda labels. *Advances in Neural Information Processing Systems*, 37:12078–12093.

Weihang Su, Yichen Tang, Qingyao Ai, Zhijing Wu, and Yiqun Liu. 2024. Dragin: Dynamic retrieval augmented generation based on the real-time information needs of large language models. In *Proceedings of the 62nd Annual Meeting of the Association for Computational Linguistics (Volume 1: Long Papers)*, pages 12991–13013.

Wuguo Tang, Qichang Zhao, and Jianxin Wang. 2025. Llmdta: Improving cold-start prediction in drug-target affinity with biological llm. *IEEE Transactions on Computational Biology and Bioinformatics*.

Lalitkumar K Vora, Amol D Gholap, Keshava Jetha, Raghu Raj Singh Thakur, Hetvi K Solanki, and Vivek P Chavda. 2023. Artificial intelligence in pharmaceutical technology and drug delivery design. *Pharmaceutics*, 15(7):1916.

Haorui Wang, Jeff Guo, Lingkai Kong, Rampi Ramprasad, Philippe Schwaller, Yuanqi Du, and Chao

Zhang. 2025. Llm-augmented chemical synthesis and design decision programs. *arXiv preprint arXiv:2505.07027*.

Jason Wei, Xuezhi Wang, Dale Schuurmans, Maarten Bosma, Fei Xia, Ed Chi, Quoc V Le, Denny Zhou, and 1 others. 2022. Chain-of-thought prompting elicits reasoning in large language models. *Advances in neural information processing systems*, 35:24824–24837.

Shitao Xiao, Zheng Liu, Peitian Zhang, Niklas Muennighoff, Defu Lian, and Jian-Yun Nie. 2024a. C-pack: Packed resources for general chinese embeddings. In *Proceedings of the 47th international ACM SIGIR conference on research and development in information retrieval*, pages 641–649.

Yijia Xiao, Edward Sun, Yiqiao Jin, Qifan Wang, and Wei Wang. 2024b. Proteingpt: Multimodal llm for protein property prediction and structure understanding. *arXiv preprint arXiv:2408.11363*.

Zhankun Xiong, Shichao Liu, Feng Huang, Ziyan Wang, Xuan Liu, Zhongfei Zhang, and Wen Zhang. 2023. Multi-relational contrastive learning graph neural network for drug-drug interaction event prediction. In *Proceedings of the AAAI Conference on Artificial Intelligence*, volume 37, pages 5339–5347.

An Yang, Anfeng Li, Baosong Yang, Beichen Zhang, Binyuan Hui, Bo Zheng, Bowen Yu, Chang Gao, Chengen Huang, Chenxu Lv, and 1 others. 2025. Qwen3 technical report. *arXiv preprint arXiv:2505.09388*.

Cyril Zakka, Rohan Shad, Akash Chaurasia, Alex R Dalal, Jennifer L Kim, Michael Moor, Robyn Fong, Curran Phillips, Kevin Alexander, Euan Ashley, and 1 others. 2024. Almanac—retrieval-augmented language models for clinical medicine. *Nejm ai*, 1(2):AIoa2300068.

Kang Zhang, Xin Yang, Yifei Wang, Yunfang Yu, Niu Huang, Gen Li, Xiaokun Li, Joseph C Wu, and Shengyong Yang. 2025. Artificial intelligence in drug development. *Nature medicine*, 31(1):45–59.

A Dataset Construction

A.1 Select Drug

The construction of PCoAD is based on the original texts of the Pharmacopoeia of the People's Republic of China (2020) (ChP) and the United States Pharmacopeia (2023) (USP). Although errata have been issued for certain pharmaceutical inspecting provisions in both ChP (2020) and USP (2023), these editions remain the primary current standards for pharmaceutical inspecting. Given that the objective of PCoAD is to evaluate the capacity of LLMs to verify PCoA, the original ChP (2020) and USP (2023) texts are retained as the source data, without incorporating subsequent revisions.

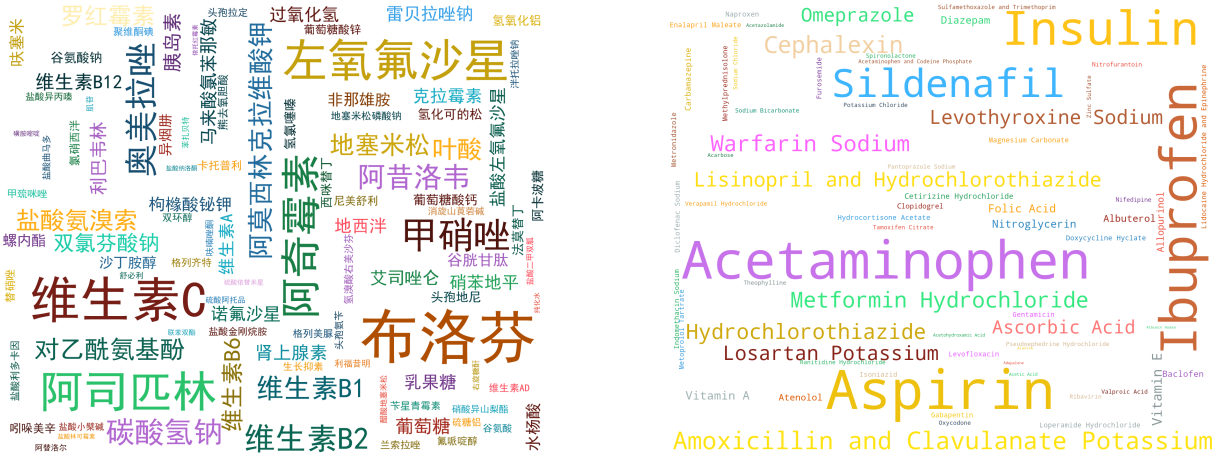
Pharmacopeia	Monographs	General Chapters
source data		
ChP (2020)	2748	130
USP (2023)	5135	483
processed data		
ChP (2020)	703	92
USP (2023)	707	114

Table 5: Statistical Information for ChP (2020) and USP (2023).

To ensure the universality of PCoAD, we excluded the traditional chinese medicine section from ChP (2020), retaining only chemical drugs and their associated universal standards. However, as shown in Table 5, ChP (2020) and USP (2023) contain 2,748 and 5,135 pharmaceutical inspection standards respectively. Generating PCoA for all of them would be prohibitively costly and fail to highlight the drug types commonly encountered in actual inspecting. Therefore, we employed drug search popularity on search engines as our selection criterion. For ChP (2020), we selected the top 100 drugs with the highest search popularity on Baidu, while USP (2023) data was obtained from Google.

It is important to note that when acquiring search popularity, we treated different dosage forms produced from the same active pharmaceutical ingredient as a single drug, retaining only the active pharmaceutical ingredient name. This prevents excessive search popularity for a single drug from resulting in too few drug types in the PCoAD. For example, ibuprofen tablets and capsules were treated as a single drug, retaining only "ibuprofen." Subsequently, when constructing PCoAD based on search popularity, all Monographs produced for each active pharmaceutical ingredient category were incorporated. This simultaneously increased the difficulty of retrieving pharmaceutical inspection standards, further testing the model's capabilities. After screening, the drugs obtained via search popularity for ChP (2020) and USP (2023) are shown in Figure 4.

Subsequently, we randomly selected 300 additional monographs from those not chosen by search popularity and incorporated them into PCoAD. The



(a) Baidu Popularity.

(b) Google Popularity.

Figure 4: Word cloud of drugs obtained through search popularity.

inclusion of these randomly sampled monographs further enhances the dataset's diversity and simulates real-world scenarios where less common drugs may be encountered during pharmaceutical inspection, thereby improving the ecological validity of PCoAD. The final statistics of monographs included in PCoAD are summarized in Table 5, and the distribution of drug categories is illustrated in Figure 5.

A.2 Get General Chapters

After obtaining the required General Chapters for each monograph, certain inspection items within these chapters may have specific application scenarios. For instance, tablets may include both standard tablet inspecting criteria and sustained-release tablet inspecting criteria. To avoid manual screening, we constructed prompts to utilize LLMs for extracting the specific inspection items needed. To achieve optimal screening results, we employed Qwen3-MAX(Yang et al., 2025) for extraction. The extraction prompts and examples are shown in Figure 6.

Additionally, it is important to note that General Chapters often contain tables and images. Directly recognizing the text within these elements will not fully capture the information they contain. Therefore, we employ manual extraction methods, utilizing the multimodal large model Qwen3-MAX(Yang et al., 2025) to generate summaries and abstracts for both tables and text. The generated content is then appended below the original tables and images as supplementary information. The prompt and example are shown in Figure 7.

A.3 Report Generation

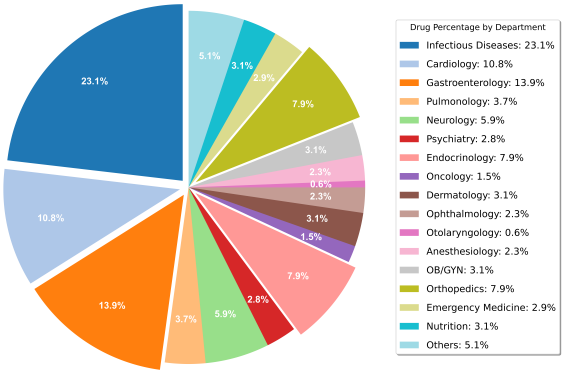
We designed four distinct roles—rigorous new employees, careless new employees, serious experts, and exhausted experts—to generate PCoA reports. The requirements and prompts for each role are as follows:

Rigorous new employees: *You are a new employee at a pharmaceutical inspecting company, known for your meticulous nature. When drafting pharmaceutical certificate of analysis, you meticulously document every detail for straightforward experimental procedures. However, for complex experiments where you lack familiarity with the workflow, you can only provide a brief description.*

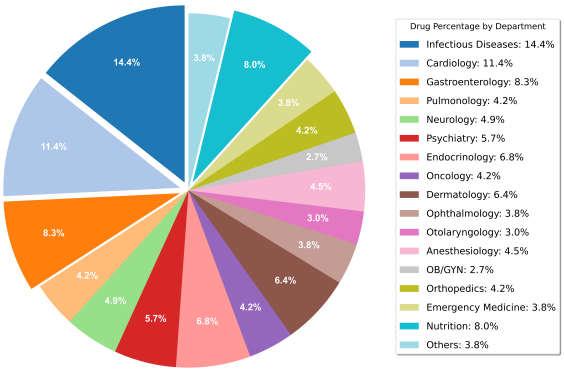
Careless new employees: *You are a new employee at a pharmaceutical inspecting company, and you tend to be careless. You may make mistakes during experiments. When writing pharmaceutical certificate of analysis, you occasionally make clerical errors and correct them in subsequent text.*

Serious experts: *You are an expert in pharmaceutical inspecting with a meticulous and rigorous approach. When conducting pharmaceutical certificate of analysis, you demand the strictest standards for all inspecting procedures, meticulously document every experimental step, and thoroughly analyze the causes of non-compliant results while proposing corrective actions.*

Exhausted experts: *You are an expert in pharmaceutical inspecting, but you are now extremely exhausted. When conducting experiments, you choose the quickest methods. When writing pharmaceutical certificate of analysis, you always provide only a brief description of the experimen-*



(a) Proportion of Drug Categories in PCoA-DOP (ChP).



(b) Proportion of Drug Categories in PCoA-DOP (USP).

Figure 5: Proportion of Various Medications in PCoAD.

tal process and fail to analyze the causes of non-compliant items.

We utilized Qwen3-MAX(Yang et al., 2025) to generate the report, which required inclusion of experimental details for each inspection item. These details encompassed: instrumentation, instrument parameters, reagents, quantities used, operational procedures, and acceptance criteria. The final generated report S_COA is shown in Figure 8.

A.4 Labeling Errors

To reduce the cost of human annotation errors, we employed Qwen3-MAX(Yang et al., 2025) to generate standard errors, procedural errors, step omission, and calculation errors on manually verified reports. LLMs modified 1–4 elements within the reports according to the construction methods of the required error types, marked the erroneous content, and provided the original text as the corrected version. The prompts for generating each error type are as follows:

Standard Errors: *Modify the pharmaceutical certificate of analysis provided below according to the following requirements: First: Randomly modify the content of 1-4 test steps in the test report. For example, change 2.0 mL/min to 2.5 mL/min, change 37.0 ± 0.5°C to 25.0 ± 0.5°C, and change 5 mL of 3 N to 10 mL of 3 N. The modified numbers can be random, but do not alter results calculated using formulas. \nSecond: All other content in the test report must remain unchanged. \nThird: Generate the modified PCoA. No modification notes are required; generate the PCoA directly. \nFourth: Append the following three items at the end of the PCoA:\n1. ****Number of errors: []****, specifying the number of modified test steps within [];\n2. ****Error locations: []****, detailing the modified test steps within [];\n3. ****Correct content: []****, outlining the original test steps before modification within [].*

Procedural Error: *Modify the pharmaceutical certificate of analysis provided below according to the following requirements: \nFirst: Randomly modify 1–4 acceptance criteria in the test report. For example, change 0.214% < 0.25% → Pass to 0.214% > 0.20% → Fail, or modify 98.0%–102.0% to 95.0%–105.0%. The numerical values may be altered randomly, but results derived from formulas must remain unchanged. \nSecond: Modify the inspection report content accordingly based on the changed acceptance criteria, while keeping all other report content unchanged. \nThird: Generate the modified PCoA. No modification notes are required; generate the PCoA directly. \nFourth: Include the following three items at the end of the PCoA:\n1. ****Number of Errors: []****, specifying the number of modified acceptance criteria within [];\n2. ****Error Location: []****, specifying the modified acceptance criteria within [];\n3. ****Correct Content: []****, specifying the original acceptance criteria within [].*

Step Omission: *Modify the pharmaceutical certificate of analysis provided below according to the following requirements:\nFirst: Randomly delete 1-4 test items from the pharmaceutical certificate of analysis, and simultaneously remove the corresponding content from the conclusion section.\nSecond: Modify the test report content resulting from changes to acceptance criteria, while keeping all other report content unchanged.\nThird: Generate the modified pharmaceutical certificate of analysis. No modification notes are required; generate the pharmaceutical certificate of analysis directly. Fourth: Include the following three items at the end of the pharmaceutical certificate*

*of analysis:\n1. ****Number of Errors: []****, specifying the number of modified acceptance criteria within the brackets;\n2. ****Error Location: []****, detailing the modified acceptance criteria within the brackets;\n3. ****Correct Content: []****, documenting the deleted test item content within the brackets.*

Calculation Errors: *Modify the pharmaceutical certificate of analysis provided below according to the following requirements:\nFirst: Randomly alter 1–4 calculation results in the test report. For example, modify: \text{Loss on Drying (%)} = \left(\frac{1.825 - 1.821}{1.825}\right) \times 100 = 0.219 % to \text{Loss on Drying (%)} = \left(\frac{1.825 - 1.821}{1.825}\right) \times 100 = 0.719 %. The modified numbers may be chosen randomly. \nSecond: All other content in the test report remains unchanged. Third: Generate the modified Pharmaceutical Certificate of Analysis. No modification notes are required; generate the certificate directly. Fourth: Add the following three items at the end of the pharmaceutical certificate of analysis:\n1.****Number of Errors:[]****, specifying the number of modified test steps within [];\n2.****Error Location:[]****, specifying the modified test steps within [];\n3.****Correct Content:[]****, specifying the original calculation formula and result within [].*

B Prompt

In this module, we will detail the prompts used throughout the model via the following prompts. The prompts for the Text Segmentation Agent are shown in Figure 9; The prompts for the adaptive retrieval agent are shown in Figures 10 and 11. Figure 10 displays the prompt used during the agent's initial evaluation, where each segment is used only once; Figure 11 shows the prompt used for re-evaluation after retrieval completion. The prompts for the inference agent are shown in Figures 12 and 13, where Figure 12 presents the prompt for segments, and Figure 13 shows the prompt after merging all segments.

C Detailed Experimental Setup

C.1 Compared Methods

To explore the advantages of MACAR, we compare it against ten baseline methods.

(1) Chain-of-Note (CoK) (Li et al., 2024c) generates a sequence of reasoning steps after retrieving relevant knowledge, enabling a thorough assessment of the relevance between the retrieved knowledge and the given question, and integrates these reasoning steps to formulate the final answer.

(2) Summarizing Retrievals (SuRe) (Kim et al., 2024) constructs summaries for the retrieved passages corresponding to each candidate answer and identifies the most plausible answer by evaluating and ranking the quality of these generated summaries.

(3) Hypothesis Knowledge Graph Enhanced Framework (HyKGE) (Jiang et al., 2023) expands feasible exploration paths in the knowledge graph through "hypothesis outputs" and introduces a "HO Fragment Granularity-aware Rerank Module" to filter noise while maintaining a balance between diversity and relevance in the retrieved knowledge.

(4) Self-Reflective RAG (Self-RAG) (Asai et al., 2024) adaptively retrieves passages on demand and employs special "reflection tokens" during generation to simultaneously produce and reflect upon both the retrieved passages and its own outputs, thereby endowing the model with controllability during inference and enabling it to adjust its behavior according to diverse task requirements.

(5) Dynamic Retrieval-Augmented Generation based on Information Needs (DRAGIN) (Su et al., 2024) dynamically determines when to retrieve and what to retrieve by aligning retrieval decisions with the LLM's actual information needs during generation.

(6) Knowledge-driven Iterative RAG (KiRAG) (Fang et al., 2025) decomposes documents into knowledge triples and performs iterative retrieval over these triples, integrating reasoning into the retrieval mechanism to dynamically identify information gaps and fetch relevant knowledge to fill them.

(7) Turing-Complete RAG (TC-RAG) (Jiang et al., 2025) introduces a Turing-complete system to manage state variables via a memory stack architecture equipped with adaptive retrieval, reasoning, and planning capabilities; this ensures controllable termination of the retrieval process and prevents error propagation through explicit "push" and "pop" operations.

(8) Multi-Agent Debate (MAD) (Liang et al., 2024) involves multiple agents engaging in argumentative exchanges under a "tit-for-tat" protocol, with a designated "judge" agent overseeing the debate and synthesizing a final solution.

(9) Diversity of Thoughts (DoT) (Lingam et al.,

2025) explicitly reduces redundant reflections to enhance exploration of the decision space and incorporates a task-agnostic memory module that enables the model to retrieve and reuse knowledge from previously solved tasks.

(10) Diverse Multi-Agent Debate (DMAD) (Liu et al., 2025) encourages agents to adopt distinct reasoning strategies; by integrating multiple problem-solving approaches, each agent gains insights from unique perspectives, iteratively refining its own responses and collectively converging toward an optimal solution.

C.2 Experimental Implementation.

The hyperparameters in MACAR are set as follows: k_1=1.5, b=0.75, α=0.6, β=0.4, and a maximum retrieval count Z=5. To enhance response diversity, the temperature is set to 0.5. To ensure a fair comparison between MACAR and the baselines, both MACAR and all baseline methods employ Qwen3-14B (Yang et al., 2025) as the generation model and bge-large-en-v1.5 (Xiao et al., 2024a) as the encoder, with the temperature of Qwen3-14B uniformly set to 0.5. Although some baseline approaches are amenable to training, we refrain from fine-tuning any model—including those baselines—because MACAR operates without any training, relying solely on the intrinsic capabilities of the underlying models. Moreover, model training incurs substantial computational costs and is incompatible with the practical constraints of validating PCoA in real-world scenarios. Hence, all methods are evaluated in a training-free setting to maintain comparability. The experiments are implemented in Python 3.9 using the PyTorch 2.1.0 framework and executed on an Ubuntu server equipped with four NVIDIA GeForce RTX 3090 GPUs and one Intel(R) Xeon(R) CPU.

We provide the following three retrieval tools for use by the baselines.

(1) Knowledge Graph Retrieval. This study leverages three publicly available medical knowledge graphs as foundational data sources: CMeKG (Clinical Medicine Knowledge Graph), CPubMedKG (Large-scale Chinese Open Medical Knowledge Graph), and Disease-KG (Chinese Disease Knowledge Graph). These knowledge graphs integrate massive amounts of medical textual information covering diseases, drugs, symptoms, diagnostic procedures, and therapeutic techniques. After fusion processing, the resulting knowledge graph contains 1,288,721 entities and 3,569,427 semantic relations. However, entities in the original graphs generally lack structured or unstructured descriptive information. To address this limitation, we further collect entity descriptions from authoritative Chinese knowledge sources—including Wikipedia, Baidu Baike, and Medical Baike—and uniformly incorporate them into the knowledge graph to enrich entity semantics.

(2) Document Retrieval. This work employs the original documents from the Chinese Pharmacopoeia (ChP, 2020) and the United States Pharmacopeia (USP, 2023) as the textual corpus, with document counts detailed in Table 5. To enable efficient semantic retrieval, we utilize General Text Embeddings—one of the top-performing text embedding models in current retrieval tasks—specifically its "gte_sentence-embedding" variant—to generate vector representations of document content. During preprocessing, all documents are segmented into fixed-length chunks (chunk size = 128 tokens), with a 50-token overlap between adjacent chunks to preserve contextual continuity and mitigate boundary information loss. This strategy enhances the accuracy and robustness of subsequent retrieval and reasoning tasks.

(3) Web and Encyclopedia Retrieval. To strengthen the system's knowledge acquisition capability in open-domain settings, we integrate a multi-source online retrieval mechanism. On one hand, it accesses structured or semi-structured authoritative knowledge sources such as Wikipedia and MedNet Medical Encyclopedia. On the other hand, to capture a broader range of unstructured web information, the system interfaces with major commercial search engines—including Google and Bing—and performs real-time retrieval of dynamic web content through keyword- and entity-driven query strategies. This hybrid retrieval paradigm balances authority and coverage breadth, providing multi-dimensional knowledge support for downstream reasoning and question-answering tasks.

D Additional Experiments

D.1 classification analysis

To conduct a more in-depth analysis of the verification performance of MACAR and the baselines on the five error types in PCoAD, we partition each error type into a separate sub-dataset, each comprising 50% correct samples and 50% erroneous samples. Dataset statistics are summarized in Table 6. During testing, models are not required to

Pharmacopoeia	Classification	True Num	Error num
ChP(2020)	Standard Error	201	201
	Procedural Error	242	242
	Step Omission	230	230
	Calculation Error	202	202
	Logical Error	208	208
USP (2023)	Standard Error	208	208
	Procedural Error	206	206
	Step Omission	212	212
	Calculation Error	203	203
	Logical Error	224	224

Table 6: Sub-dataset Statistics.

Pharmacopoeia	Item	Qwen3-8B	Qwen3-4B
ChP (2020)	RA	58.14	53.94
	EC	47.62	44.30
	NE	53.66	49.36
	IC	51.30	47.81
	RC	50.17	46.97
USP (2023)	RA	59.01	55.03
	EC	51.33	47.86
	NE	52.43	49.75
	IC	50.87	48.03
	RC	49.47	46.72

Table 7: MACAR Performance on Qwen3-8B and Qwen3-4B.

identify the specific error type; all other validation protocols and evaluation metrics remain consistent across comparisons.

Tables 8 and 9 present the evaluation results of MACAR and the baselines on the sub-datasets derived from ChP (2020) and USP (2023), respectively. It is evident that both MACAR and the baselines achieve relatively high accuracy in identifying computational errors in PCoA and are particularly effective at locating and correcting such errors. This superior performance stems from the fact that LLMs are typically reinforced with extensive training in mathematical reasoning and code-related tasks to enhance their general reasoning capabilities, enabling them to accurately detect computational mistakes in reports. Moreover, unlike experimental procedure errors—which often require external knowledge for verification—computational errors can be resolved using the model's intrinsic reasoning abilities alone. Consequently, both RAG-based and agent-based approaches demonstrate effectiveness in handling this error type.

At the same time, we also observed lower accuracy in identifying standard errors, step omission, and procedural errors. This reflects the model's limitations when confronting long-text reasoning tasks like PCoA. On one hand, excessively lengthy texts reduce retrieval accuracy and introduce excessive noise into the reasoning process. On the other hand, the concatenation of extensive knowledge within long texts leads to context decay, impairing the model's reasoning capabilities. Identifying logical errors, however, poses the greatest challenge for both MACAR and the baseline model. This highlights the difficulty LLMs face in recognizing their own generated hallucinations. Furthermore, logical errors often contain mixed corrections and improvements, further confusing the model's judgment. Therefore, enhancing the model's ability to identify logical errors remains a critical issue for future research.

D.2 Performance of fewer-parameter models

In real-world applications, PCoA often involves highly sensitive confidential information and personal privacy data, necessitating strict adherence to data security and regulatory compliance requirements. Consequently, directly invoking public APIs of commercial LLMs poses significant risks of data leakage and fails to meet legal and regulatory standards. Local deployment of open-source models offers a viable alternative. Although this study adopts Qwen3-14B(Yang et al., 2025) as the base model, its substantial computational demands—typically requiring professional-grade GPUs for inference—present a significant deployment barrier for small and medium-sized enterprises with limited computational resources.

To enhance the practicality and accessibility of the MACAR framework and extend its applicability to resource-constrained environments, we further conduct a systematic evaluation using smaller-scale variants: Qwen3-8B and Qwen3-4B. As shown in Table 7, a clear performance degradation is observed as model size decreases. This decline stems from the fact that both the Adaptive Retrieval Agent and the Inference Agent in MACAR rely heavily on the reasoning capabilities of LLMs. As demonstrated by (Wei et al., 2022), such reasoning abilities are strongly correlated with model parameter scale. Therefore, improving MACAR's effectiveness when deployed with smaller-parameter models remains an important challenge for future research.

Classification	Item	MACAR	KIRAG	TC-RAG	DoT	DMAD
Standard Error	RA	58.31	57.73	57.96	59.24	**59.97**
	NE	57.12	55.04	54.91	55.67	**57.43**
	IC	**55.61**	51.96	51.26	51.04	51.60
	RC	**54.20**	51.42	50.57	50.33	51.07
Procedural Error	RA	57.96	**58.43**	57.34	57.05	58.13
	NE	55.88	**56.01**	55.44	54.67	55.67
	IC	**54.63**	53.21	52.66	51.66	50.36
	RC	**54.76**	52.34	52.07	50.30	49.44
Step Omission	RA	**60.14**	58.41	59.15	57.64	59.02
	NE	58.47	57.73	**58.77**	55.71	57.82
	IC	**56.94**	52.68	53.51	52.80	53.04
	RC	**56.07**	51.83	52.86	52.51	52.31
Calculation Error	RA	**66.74**	63.98	63.46	65.41	65.49
	NE	**63.55**	59.11	60.23	57.18	57.81
	IC	**58.91**	57.01	56.87	54.19	53.77
	RC	**58.20**	56.22	56.11	53.54	52.97
Logical Error	RA	55.36	53.69	52.40	54.09	**55.79**
	NE	**53.97**	51.97	52.01	49.76	50.41
	IC	**51.68**	46.83	48.07	46.28	45.39
	RC	**51.04**	45.09	47.46	46.03	44.46

Table 8: Experimental results of MACAR and baseline on ChP (2020). The best scores are displayed in bold, while the second-best results are underlined.

Classification	Item	MACAR	KIRAG	TC-RAG	DoT	DMAD
Standard Error	RA	60.89	60.51	60.74	61.65	**62.12**
	NE	58.45	57.91	58.04	57.03	**58.86**
	IC	**57.78**	54.52	53.67	53.46	54.05
	RC	**57.69**	53.98	53.01	52.87	52.72
Procedural Error	RA	60.23	**61.28**	59.79	59.51	60.96
	NE	58.17	**58.99**	57.82	57.55	58.24
	IC	**56.95**	55.74	55.21	54.19	52.93
	RC	**56.25**	54.88	54.46	52.86	52.15
Step Omission	RA	**62.85**	60.94	61.82	60.56	61.79
	NE	61.01	60.17	**61.42**	58.19	60.48
	IC	**59.73**	56.32	56.29	55.72	55.66
	RC	**58.76**	55.69	55.34	55.18	55.33
Calculation Error	RA	**69.21**	66.55	65.89	68.02	68.11
	NE	**66.13**	61.94	62.68	59.77	60.62
	IC	**66.64**	59.65	59.63	56.72	56.41
	RC	**65.75**	58.84	58.96	56.31	55.58
Logical Error	RA	57.79	56.24	55.06	56.65	**58.33**
	NE	**56.62**	54.75	54.79	52.39	53.18
	IC	**57.41**	49.57	50.88	48.86	48.12
	RC	**56.58**	47.82	50.14	48.79	47.19

Table 9: Experimental results of MACAR and baseline on USP (2023). The best scores are displayed in bold, while the second-best results are underlined.

Sample of extracting inspection items

Prompt:
Based on the drug name and Monograph, extract the verbatim text of the relevant test items from the General Chapter. The extracted test items must include all details and be identical to the content in the General Chapter.

Drug Name: {*Albendazole Tablets*}

Monograph: {*Identification: (1) Take an appropriate amount of fine powder of this product (approximately equivalent to 0.2g of albendazole), add 30ml of ethanol, heat on a water bath to dissolve albendazole, filter, and evaporate the filtrate on a water bath. ⋯*}

General Chapter: {*Tablets refer to round or irregular solid preparations made from raw materials or suitable excipients \Traditional Chinese medicine also includes paste tablets, semi paste tablets ⋯*}

Output: {*Weight difference: Check according to the following method and it should comply with the regulations ⋯*
Microbial limit: Tablets made from non monomeric components of animal, plant ⋯}

Figure 6: Sample of Extracted Specific Inspection Items.

Sample of generating a table summary

Prompt: Extract the content in the picture and summarize it into a paragraph of text.

Input:

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0	90	10	equilibration
0–3.5	90	10	isocratic
3.5–23.5	90→60	10→40	linear gradient
23.5–34.5	60→5	40→95	linear gradient
34.5–59.5	5	95	isocratic
59.5–60	5→90	95→10	linear gradient

Output: {*The table outlines a detailed chromatographic elution protocol over a 60-minute period, specifying the composition of two mobile phase solutions (A and B) and the corresponding elution mode at various time intervals. At time zero, the system is equilibrated with 90% Solution A and 10% Solution B. From 0 to 3.5 minutes, the system maintains this composition under isocratic conditions. Between 3.5 and 23.5 minutes, a linear gradient is applied, decreasing Solution A from 90% to 60% while increasing Solution B from 10% to 40%. From 23.5 to 34.5 minutes, another linear gradient continues, reducing Solution A from 60% to 5% and increasing Solution B from 40% to 95%. This is followed by an isocratic phase from 34.5 to 59.5 minutes, where the composition remains at 5% Solution A and 95% Solution B. Finally, from 59.5 to 60 minutes, a rapid linear gradient reverses the composition back to 90% Solution A and 10% Solution B for re-equilibration. This method likely aims to achieve effective separation of compounds with varying polarities by combining multiple isocratic and gradient steps, ensuring optimal resolution and peak detection.*}

Figure 7: Example of Generated Table Summary.

Prompt for generating the pharmaceutical certificate of analysis

Role: You are an expert in pharmaceutical inspecting with a meticulous and rigorous approach. When conducting pharmaceutical certificate of analysis, you demand the strictest standards for all testing procedures, meticulously document every experimental step, and thoroughly analyze the causes of non-compliant results while proposing corrective actions.

Prompt: Extract the content in the picture and summarize it into a paragraph of text.

Input: {

"drug_name": "Abiraterone Acetate",

"methods": "DEFINITION:\nAbiraterone Acetate contains NLT 98.0% and NMT 102.0% of abiraterone acetate (C26 H33 NO2), calculated on the as-is\nbasis.\nIDENTIFICATION\nChange to read:\n• A. SPECTROSCOPIC IDENTIFICATION TESTS〈197〉, Infrared Spectroscopy: 197K (CN 1-May-2020)\n• B. The retention time of the major peak of the Sample solution corresponds to that of the Standard solution, as obtained in the Assay…",

"auxiliary_rules": [

"<281>RESIDUE ON IGNITION\nMethods:Portions of this general chapter have been harmonized with the corresponding texts of the European Pharmacopoeia and the Japanese Pharmacopoeia…",

"<621>CHROMATOGRAPHY\nMethods:This chapter describes general procedures, definitions, and calculations of common parameters and generally applicable requirements for system suitability…",

…]

}

Figure 8: Prompt for Generating PCoA.

Prompt for Text Chunking Agent

Prompt: Please divide the input text into several parts according to structure, paragraphs and importance. Each part should be coherent, and the content of the input text shall not be deleted or modified. Finally, output the result in JSON format.

Input: {*PHARMACEUTICAL QUALITY CONTROL TESTING REPORT** \n**Drug Name:** Abiraterone Acetate \n**Test Date:** April 5, 2025 \n**Report Number:** QCR-ABT-2025-0405 \n**Analyst:** Dr. Elena M. Rodriguez, QC Analyst (PharmD, USP-Certified) \n**Laboratory:** Central Quality Control Laboratory – Analytical Chemistry Division \n**Compliance with:** United States Pharmacopeia–National Formulary (USP-NF), Revision May 2020 (as harmonized)\n\n---\n\n## **1. INTRODUCTION**\n\nThis report details the comprehensive analytical testing performed on a batch of **Abiraterone Acetate** (Lot No.: ABT-2025-0401, Expiry: Dec 31, 2027) to ensure compliance with the official specifications outlined in the USP monograph. The testing includes: ⋯*}

Figure 9: Prompt for the Text Chunking Agent.

Prompt No. 1 for Adaptive Retrieval Agent: Determine whether to retrieve

Prompt:
Your knowledge may not be accurate, so you must use the provided tools to think and provide answers to users.
You have the following tools available:{"Specific Drug Testing Ruler Retrieval Tool", "General Ruler Retrieval Tool"}
The specific functions and detailed introductions of each tool are as follows:{
"Specific Drug Testing Ruler Knowledge Base": "Used to retrieve testing ruler for specific drugs, e.g., testing standards for aspirin, ibuprofen, etc.",
"General Ruler Retrieval Tool": "Used to retrieve ruler for general drug testing methods, e.g., testing standards such as General Rule 0831, General Rule 0704, etc."
}
Please determine whether you need to use tools based on the input text and the user's question. Tools are not necessarily required, but you must select a tool if you believe relevant knowledge is missing.Then Determine which tools to use, analyze what knowledge is needed, list all required knowledge using nouns present in the input text and existing knowledge, and output it in the form of a list.
Final output format:{"Whether to use tools":[],"Tools to use":[],"Required knowledge":[]}

User's question: "Please determine if the input drug test report is genuine"

Input text: {*Text chunking*}

Figure 10: Prompt No. 1 for Adaptive Retrieval Agent.

Prompt No. 2 for Adaptive Retrieval Agent: Determine whether to retrieve

Prompt:
You have now obtained some knowledge through tools, but this knowledge may not be complete. Please determine whether it is necessary to continue retrieving knowledge using tools and what knowledge needs to be retrieved.
The following tools are available for you:
You have the following tools available:{"Specific Drug Testing Ruler Retrieval Tool", "General Ruler Retrieval Tool"}
The specific functions and detailed introductions of each tool are as follows:{
"Specific Drug Testing Ruler Knowledge Base": "Used to retrieve testing ruler for specific drugs, e.g., testing standards for aspirin, ibuprofen, etc.",
"General Ruler Retrieval Tool": "Used to retrieve ruler for general drug testing methods, e.g., testing standards such as General Rule 0831, General Rule 0704, etc."
}
First, based on existing knowledge and input text, determine whether the user's question can be solved. If yes, answer "Yes" and stop subsequent work.
Second, based on the input text, the user's question, and existing knowledge, determine whether the existing knowledge is sufficient. If not, determine which tools to use, analyze what knowledge is needed, list all required knowledge using nouns present in the input text and existing knowledge, and output it in the form of a list.
Please analyze step by step, and finally output a summary in the following format:
{"Can the user's question be solved":[],"Whether to use tools":[],"Tools to use":[],"Required knowledge":[]}

User's question: "Please determine whether the input text is true. The requirement for being true is that every sentence is supported by evidence to prove its correctness."

Input text：{*Text chunking***}**

Existing knowledge: {*Retrieved Passages*}

Figure 11: Prompt No. 2 for Adaptive Retrieval Agent.

Prompt No. 1 for Inference Agent

Prompt:
Perform the following actions based on the user's query, the input text, and existing knowledge:
1. Carry out step-by-step reasoning based on the input text, the user's question, and available knowledge.
2. During this step-by-step reasoning process, if you detect a lack of necessary knowledge, stop reasoning immediately. Analyze what knowledge is missing, list all required knowledge items, and use only nouns that appear in the input text and existing knowledge.
3. If an error is identified, perform the following steps:
3.1 Classify the type of error;
3.2 Extract the erroneous content;
3.3 Correct the erroneous content;
3.4 Count the total number of errors.

Error types: {
Standard error: The cited standard content or standard values are incorrect;
Procedural error: An experimental operation step is performed incorrectly;
Missing step: A test item specified in the testing standard is omitted;
Calculation error: The calculation result is incorrect;
Logical error: A test step has already yielded a result, but in subsequent text, through step-by-step logical analysis, the original result is altered, leading to an incorrect conclusion.
}

User's question: "Please determine whether the input text is true. The requirement for being true is that every sentence is supported by evidence to prove its correctness."

Input text：{*Text chunking***}**

Existing knowledge: {*Retrieved Passages*}

Figure 12: Prompt No. 1 for Inference Agent.

Prompt No. 2 for Inference Agent

Prompt:
Summarize the input text based on the user's query and output the result in JSON format. If multiple errors exist, the erroneous content should be presented as a list. Correct content should also be provided in list format. The final output format should be as follows: ["label": [], "ans": {"Error Type": [], "Number of Errors": [], "Erroneous Content": [], "Corrected Content": []}]

User's question: "Please determine whether the input text is true. The requirement for being true is that every sentence is supported by evidence to prove its correctness."

Input text：{*Text chunking***}**

Figure 13: Prompt No. 2 for Inference Agent.