

Research on the Quality Status Analysis of Chinese Patent Medicines in National Drug Sampling Inspection

Abstract

To scientifically evaluate the quality risks of non-conforming Chinese patent medicines and establish a differentiated regulatory approach, this study is based on the inspection data of Chinese patent medicines from the National Drug Sampling Inspection conducted between 2020 and 2024. The distribution characteristics of non-conforming items were statistically analyzed, and risk-stratified assessment was performed by combining the results of routine testing and exploratory research. The results showed that the overall quality of Chinese patent medicines has maintained a steady upward trend. Identification, assay, related substances, dissolution, and microbial limits — as the core testing modules of pharmacopoeial standards — control the authenticity of the herbal prescription, the level of active pharmaceutical ingredients, impurity safety, in-vitro release behavior of the preparation, and microbial contamination risk, respectively. Non-conformity in any of the above items constitutes a substantive high-risk defect that may directly threaten medication safety and clinical efficacy. Some sampled products exhibited deviations in appearance and description without altering the intrinsic material basis of the medicines, posing a relatively low risk to actual clinical use. Quality hazards in Chinese patent medicines are mainly concentrated in inconsistent quality of Chinese herbal medicine raw materials, weak control over extraction and manufacturing processes, and enterprise quality control systems that exist in name only.

Keywords: Chinese patent medicine; sampling inspection; non-conformity; quality risk

1 Introduction

A complete quality standard for Chinese patent medicines consists of four major components: description, identification, examination, and assay. Among these, the description (character) serves as the fundamental visual inspection item, encompassing sensory indicators such as color, form, odor, and texture, used to preliminarily evaluate the batch-to-batch consistency in physical appearance. Identification verifies the authenticity of the herbal ingredients in the formulation; the assay monitors the actual levels of active or marker components; and examination represents the largest category of tests, covering multiple sub-

items including related substances, dissolution, weight variation, disintegration time, and microbial limits — each controlling distinct risks such as impurities, in-vitro release characteristics, dosage form processing, and microbial contamination. In previous rounds of national drug sampling inspections, the non-conformance rate for description has been relatively high, drawing regulatory attention. However, in practice, there is a tendency to overemphasize description results while overlooking intrinsic test data, treating minor appearance flaws as equivalent to substantive quality deterioration. Without risk differentiation among different non-conforming items, this approach may lead to risk misjudgment and homogenized disposal measures.

To further refine quality risk classification for Chinese patent medicines, this study conducted a systematic analysis based on national sampling big data from 2020 to 2024, integrating the results of description, identification, assay, related substances, dissolution, microbial limits, and other test items, comparing the differing consequences of non-conformity across inspection categories, and providing data support for differentiated regulation and scientific risk assessment of Chinese patent medicines.

2 Materials and Methods

The study used inspection data of Chinese patent medicines from the national drug sampling program between 2020 and 2024, compiling annual non-conforming item types, sample sources, distribution patterns, and findings from exploratory quality research. All inspection items were classified into two categories: appearance/description items and intrinsic quality test items. Appearance items encompassed drug description (color, form, odor, and texture); intrinsic quality test items included identification, assay, and key indicators under examination such as related substances, dissolution, and microbial limits.

Non-conforming samples were divided into two major categories: those with intrinsic quality non-conformity and those with appearance/description non-conformity only. The risk levels, harm consequences, and contributing factors of different defects were compared across three dimensions: safety, efficacy, and stability.

3 Results and Analysis

3.1 Overall Quality Status of Chinese Patent Medicines

National sampling data from 2020 to 2024 showed that the overall quality of Chinese patent medicines in China has continued to improve. The vast majority of sampled products met

pharmacopoeial requirements, and no systemic or large-scale quality safety incidents were identified across the industry. The standardization level of the entire supply chain — including raw material control, manufacturing process control, and enterprise quality assurance systems — has been continuously enhanced. However, from the perspective of non-conforming item composition, the contributing factors and severity of harm varied considerably across inspection categories, and the risk consequences of different non-conforming items differed markedly. Non-conformities in Chinese patent medicines encompassed both intrinsic quality defects — such as identification, assay, related substances, dissolution, and microbial limits under examination — and some description-related non-conformities. Non-conformity in identification typically indicated deficiencies in the authenticity of herbal ingredient sourcing, directly undermining the material basis of the preparation. Multiple sub-items under examination corresponded respectively to impurity safety risks, manufacturing process deficiencies, and microbial contamination hazards. Non-conformity in the assay was directly associated with clinical efficacy. Although description-related non-conformities occurred from time to time, many represented only minor deviations in color or appearance that were not accompanied by abnormalities in intrinsic quality indicators.

Table 1. Annual National Sampling Inspection Results for Chinese Patent Medicines (2020–2024)

Year	No. of Varieties	Batches Inspected	Non-conforming Batches	Non-conforming Rate (%)
2020	48	6338	34	0.54
2021	46	6380	20	0.31
2022	47	5805	38	0.65
2023	43	5584	29	0.52
2024	48	6684	9	0.13

Data source: National Medical Products Administration, Drug Supervision and Statistics Annual Report (2020–2024)

3.2 Clearly Stratified Risk Levels of Non-conforming Items

The description of Chinese patent medicines encompasses four sensory inspection dimensions: color, form, odor, and texture. Although description itself is a sensory test and most minor deviations represent low-risk appearance defects, different types of description abnormalities may correspond to different levels of intrinsic quality deterioration. Some description changes may serve as signals of product degradation and carry a significantly higher

risk level. However, description serves only as a preliminary quality indicator, and the final risk assessment must be based on a comprehensive evaluation of intrinsic test items such as identification, assay, related substances, and microbial limits.

Odor non-conformity carries a high-to-moderate risk level. Odor indicators derive from the volatile components of Chinese herbal medicines and represent a relatively sensitive marker of deterioration. Non-conformity manifests primarily as fading or disappearance of the characteristic odor, or the emergence of abnormal odors such as musty, sour/rancid, oxidized (har), or pungent/stimulating smells. When musty, sour, or rancid odors are detected, this often indicates mold growth, lipid oxidation, or extensive microbial proliferation. Even in the absence of visible abnormalities, microbial limit exceedance or elevated related substance levels may be present, representing genuine safety hazards. Conversely, a slight fading of the characteristic herbal aroma is typically caused by natural volatilization of volatile components during storage; if the assay, impurity, and microbial limit results are all within specifications, this constitutes a low-risk finding.

Texture non-conformity carries a moderate-to-low risk level, assessed by touch and mechanical evaluation. Non-conformity manifests as abnormal softening, caking, or excessive hardness of pills; loose or friable tablets; or hardened, water-exuding plasters. Softening and caking due to moisture absorption indicate excessive storage humidity, with secondary risk of mold growth and microbial proliferation, warranting attention to potential changes in microbial and related substance levels — a moderate risk. Minor fluctuations in hardness alone, in the absence of moisture absorption, mold growth, and with all intrinsic tests compliant, generally result from minor process variations during drying and represent low-risk appearance deviations.

Color non-conformity carries a low-to-moderate risk level and is the most common type of description non-conformity in Chinese patent medicines. It manifests primarily as colors being slightly darker, lighter, or uneven, or the appearance of spots or discoloration. When localized mold spots, abnormal black spots, or pronounced brown-to-black discoloration are present, this suggests oxidative deterioration or mold colonization — a moderate risk requiring verification of microbial limits and related substances. When only slight overall color variation or minor batch-to-batch unevenness is observed without mold spots, this is largely attributable to raw material batch differences or minor fluctuations in drying and coating processes; with all intrinsic indicators within specifications, this is generally classified as low-risk.

Form non-conformity carries the lowest overall risk, primarily assessing the physical integrity of the preparation. Non-conformity manifests as irregularly shaped pills, chipped or

deformed tablets, or clumped granules. Form abnormalities mostly originate from physical forces during molding, coating, or transport-related vibration and impact. In the absence of concurrent moisture absorption and mold growth, irregularities or defects in physical form alone generally do not alter the chemical composition, impurity levels, or microbial status of the product and represent the lowest overall risk. However, when clumping is accompanied by moisture absorption and tackiness, the risk level rises accordingly.

In summary, the severity ranking of the four description non-conformity categories, from highest to lowest, is approximately as follows: odor non-conformity with mold, rancidity, or other abnormal odors represents the highest risk, followed by texture abnormalities such as moisture-induced softening and caking, and color abnormalities such as mold spots or browning; simple color variation and physical form defects represent the lowest risk. However, description serves only as a sensory indicator — regardless of the category, no single description non-conformity can independently determine the overall product risk. Comprehensive risk assessment must integrate the results of identification, assay, related substances, microbial limits, and other intrinsic test items.

Identification serves as the first checkpoint for product authenticity, employing multiple methods including thin-layer chromatography (TLC), microscopic identification, and physicochemical identification. Microscopic identification observes powder tissue cell characteristics, while TLC compares spot patterns against reference herb and reference substance standards to confirm whether the formulation contains the prescribed herbal ingredients. Non-conformity in identification typically manifests as missing spots or microscopic features inconsistent with the prescription, indicating issues such as herbal ingredient adulteration, substitution, under-dosing, or complete omission of prescribed herbs. Once identification fails, the authenticity of the formulation can no longer be assured, undermining the material basis of the Chinese patent medicine at its source. Even if subsequent assay and impurity tests are within specifications, such findings cannot confirm the product as a qualified preparation.

Assay is primarily used to determine the content of active or marker components in the formulation, predominantly by high-performance liquid chromatography (HPLC). Due to the inherent variability of Chinese herbal medicine raw materials, component levels exhibit a reasonable fluctuation range, and pharmacopoeial standards set both upper and lower limits. Non-conformity in the assay includes both low and high content scenarios: low content directly leads to insufficient clinical dosing and diminished therapeutic effect, potentially delaying patient treatment; excessively high levels of certain components may increase the incidence of adverse

reactions. Even when appearance is entirely normal, sub-standard active ingredient levels represent a core indicator directly linked to clinical efficacy.

Related substances, as impurity control items under examination, primarily detect impurities introduced during manufacturing, inherent herbal impurities, and degradation products generated through oxidation and hydrolysis during storage. Chinese patent medicines have complex compositional systems, and some degradation products possess potential toxicity. Non-conformity in related substances means that individual or total impurity levels exceed pharmacopoeial thresholds. Such defective samples may have compliant description and assay results, but with ongoing impurity accumulation, long-term use may pose potential safety hazards to patients. This represents a relatively insidious safety risk that cannot be identified by visual inspection alone.

Dissolution is a critical examination item for oral solid dosage forms such as tablets and capsules, simulating the gastrointestinal environment to determine the rate and extent of drug release from the preparation. Some samples may have compliant assay results, but unreasonable granulation, compression, or coating processes may prevent adequate drug dissolution. Products with non-conforming dissolution experience impaired drug release in the body, resulting in decreased bioavailability — the phenomenon of “sufficient active ingredient, but the body cannot absorb it” — directly diminishing clinical efficacy. This defect similarly does not manifest in the product’s appearance.

Microbial limits, also under examination, are safety control indicators governing total bacterial count, mold and yeast count, and the presence of pathogenic microorganisms. Chinese patent medicines contain abundant plant-derived nutrients; if production cleanroom standards are inadequate, material sterilization is insufficient, or packaging seal integrity is compromised, microbial proliferation can readily occur. Products with non-conforming microbial limits pose gastrointestinal infection risks, particularly for elderly patients, children, and immunocompromised individuals; in severe cases, systemic infection may result. Some microbially contaminated samples may show no visible abnormalities in appearance or description, rendering sensory detection unreliable.

Non-conformity in any one of identification, assay, related substances, dissolution, or microbial limits constitutes a substantive quality defect directly concerning the safety and efficacy of the medicine.

In contrast, some samples exhibited only minor description non-conformity such as slightly uneven color or slight color variation between batches, while all intrinsic test items —

identification consistent with the prescription, assay within the specified range, related substances within acceptable limits, dissolution meeting release requirements, and no microbial contamination detected — were fully compliant. Such products had authentic ingredient sourcing, controlled impurity levels, normal in-vitro release, and no microbial contamination, exhibiting only minor normative deviations in appearance without any intrinsic material deterioration. The overall risk to medication safety and efficacy was low.

3.3 Analysis of Quality Issue Contributing Factors

Non-conformity in high-risk intrinsic items generally stems from systemic control deficiencies throughout the entire chain of raw materials, manufacturing, and storage.

Chinese herbal medicines originate from diverse sources and production areas. Some enterprises exercise insufficient scrutiny during procurement, acquiring adulterated or deteriorated materials, directly causing identification non-conformity. Improper harvesting and processing result in low marker component levels in the raw materials, leading to insufficient dosing and subsequent assay non-conformity.

During manufacturing, unreasonable extraction process parameters, inadequate impurity removal during purification, or material degradation due to heat or light exposure can directly cause related substance exceedance. Fluctuations in granulation, compression, or coating process parameters, or unreasonable excipient ratios, can alter the dissolution behavior of solid preparations, resulting in dissolution non-conformity.

Non-conforming cleanroom classification, irregular operator practices, insufficient material sterilization, and packaging seal defects can allow moisture and microbial ingress during storage and transport, resulting in microbial limit exceedance. These issues indicate systemic vulnerabilities in the enterprise quality management system, representing systemic risk.

Description non-conformity, by contrast, is predominantly caused by minor fluctuations in drying temperature and duration, subtle differences in coating powder composition, or small environmental temperature and humidity variations during storage — factors that alter the visible characteristics of the product without changing the authenticity of herbal ingredient sourcing, without affecting active ingredient levels, without generating abnormal impurities, without disrupting drug dissolution behavior, and without introducing microbial contamination. The intrinsic material basis of the medicine remains unchanged, and such defects carry virtually no risk to safety or efficacy.

4 Discussion

Description is merely a preliminary sensory screening indicator with inherent subjective limitations and cannot be used to infer the authenticity of identification, the level of active ingredients, the extent of impurity levels, the dissolution performance of the preparation, or the degree of microbial contamination. In practice, cases exist where samples appear normal in description but have related substance exceedance, dissolution non-conformity, or microbial contamination; conversely, samples with minor appearance flaws may have all intrinsic test items fully compliant with pharmacopoeial standards. Therefore, quality evaluation of Chinese patent medicines must integrate identification, assay, and examination items — including related substances, dissolution, and microbial limits — to form a complete chain of evidence. Product quality cannot be determined solely by description results.

In current regulatory practice, some disposal approaches treat all non-conforming items equally, applying identical measures to minor description non-conformity and to issues such as related substance exceedance or identification fraud. Such homogenized responses fail to match the actual risk stratification characteristics of Chinese patent medicines. When a Chinese patent medicine exhibits only minor description non-conformity while all intrinsic quality indicators — identification, assay, related substances, dissolution, and microbial limits — meet pharmacopoeial requirements, no substantive harm to clinical safety or efficacy is expected. Such defects are low-risk appearance deficiencies and fundamentally distinct from overall product quality deterioration.

5 Conclusions and Recommendations

5.1 Conclusions

Different inspection items for Chinese patent medicines correspond to markedly different quality risk levels. Non-conformity in identification indicates uncertainty regarding the authenticity of ingredient sourcing; non-conformity in the assay directly compromises clinical efficacy; non-conformity in related substances presents an impurity toxicity hazard; non-conformity in dissolution reduces drug bioavailability; and non-conformity in microbial limits presents an infection risk. All of the above constitute high-risk substantive defects. In contrast, samples exhibiting only minor description deviations while all intrinsic indicators — identification, assay, related substances, dissolution, and microbial limits — meet specifications have only appearance flaws with no substantive adverse impact on safety or efficacy. Quality evaluation of Chinese patent medicines must not be limited to sensory description inspection but

should integrate the full set of pharmacopoeial test items for comprehensive risk assessment.

5.2 Recommendations

Strengthen enterprise primary responsibility. Enterprises should be urged to strictly enforce incoming quality acceptance of Chinese herbal medicine raw materials and strengthen identification screening of incoming materials. Key process parameters for extraction, purification, and final product formation should be optimized to maintain consistent control over content levels and related substance impurity profiles. In-process controls for dissolution of solid preparations should be improved. Cleanroom management during production should be reinforced to ensure controllable microbial limits. On the basis of ensuring that core indicators — identification, assay, related substances, dissolution, and microbial limits — remain consistently within specifications, efforts should simultaneously be made to improve batch-to-batch consistency of product appearance, thereby comprehensively elevating the quality of Chinese patent medicine products.

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