EXPLORING THE DIVERGENCE IN CLINICAL TRIAL DESIGN, APPROVAL PATHWAYS AND CLINICAL OUTCOMES IN TELEMEDICINE: A CASE STUDY OF A REMOTE VIDEO-OTOSCOPIC IMAGING DEVICE IN TELEHEALTH APPLICATIONS

Summary of the Ph.D. Thesis

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2025

Papers related to the subject of the dissertation

I. **Pannonhalmi Á**, Posta B, Perényi Á, Rovó L, Bende B, Katona G, Csóka I, Kemény L, Szakács L. Clinical validation of a video-otoscopy-based medical device for the remote diagnosis of ear complaints. Sensors 2025; 25(3): 758. (Q1, IF: 3.5)

II. **Pannonhalmi Á**, Sipos B, Kurucz RI, Katona G, Kemény L, Csóka I. Advancing regulatory oversight of medical device trials to align with clinical drug standards in the European Union. Pharmaceuticals 2025; 18(6): 876. (Q1, IF: 4.8)

III. Bende B, **Pannonhalmi Á**, Németh A, Miglinci L, Kemény L. A transzlációs medicina aktuális kérdései a mai magyar bőrgyógyászatban. Beavatkozással járó, vizsgálói kezdeményezésű klinikai vizsgálatok kivitelezésének jó gyakorlata. BVSZ 2019; 95(6): 267.

IV. **Pannonhalmi Á**, Bende B, Szakács L. Clinical validation of video-otoscopy based medical device for remote diagnosis of ear complains. V. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science. January 18-20, 2023 - Szeged, Hungary. Book of Abstracts 2023; FP-07: 62.

V. **Pannonhalmi Á**, Vass A, Bende B, Csóka I, Kemény L. Patient safety issues in telemedicine application development in case of peripheral arterial disease. 4th International Conference on Pharmaceutical and Medical Sciences. September 16-18, 2022 - Martin, Kraków, Szeged. Conference Book 2022; 90-91.

1. Introduction

The global market for drugs and medical devices is a rapidly evolving sector of the pharmaceutical industry, directly affecting daily interpretation and utilization of innovations in healthcare, academic research, and economic development. Clinical trials are a cornerstone of evidence-based medicine, which forms the basis for approval and integration of novel therapeutic interventions into routine clinical practice. Over the past decades, the methodological landscape of clinical trials has evolved remarkably, especially in the domains of pharmaceuticals and medical devices. Whilst clinical trials for drug development are guided by well-established, straightforward regulatory frameworks and standardized protocols, medical devices pose a more challenging area due to the variability in this product category, which is shaped by the inherent complexity and variability of device design, human factors, and user interactions.

Telemedicine is a rapidly growing field in daily clinical practice that leverages digital communication technologies to deliver healthcare remotely, introducing unprecedented flexibility in patient-provider interactions. The main advantage of telemedicine stems from its ability to merge healthcare services with information technology through distinctive user interfaces and remote diagnostic capabilities, and asynchronous data exchange methods. The transition to telemedicine introduces new variables, which include connectivity issues and device usability problems, and patient digital literacy challenges that do not exist in conventional face-to-face healthcare delivery. The distinctive features of telemedical trials need to be recognized as separate from standard clinical trials. Telemedical interventions need distinct outcome measures and decentralized trial designs and must address confounders that stem from technology use. The evolving regulatory, ethical, and logistical frameworks for telemedicine require trial designs that properly address its unique operational and clinical characteristics. Telemedicine is particularly important in otorhinolaryngology due to the high prevalence of conditions that can be initially assessed through visual and auditory examination, such as ear infections. It enables timely access to specialist evaluation, particularly in remote areas where in-person otolaryngology services are limited.

Understanding how clinical trials for various product categories and how telemedical devices differ from traditional drug trials, especially in terms of design, regulation, and implementation. Evaluating a novel telemedical device contributes to the advancement of accessible, high-quality ear care and supports the broader integration of telemedicine in routine practice.

1.1.Summary of regulation of clinical trials in the European Union

The Clinical Trials Regulation (CTR) No. 536/2014 functions as the main European Union legislative framework which unifies clinical trial authorization and conduct and supervision procedures throughout EU Member States. The Clinical Trials Regulation (CTR) No. 536/2014 became operational in January 2022 after replacing the Clinical Trials Directive (2001/20/EC). The Clinical Trials Information System (CTIS) functions as a centralized EU portal and database which provides sponsors with a unified entry point while enabling coordinated assessments between Member States. The regulation provides defined timeframes for evaluation and authorization procedures while making trial data accessible to the public and strengthening participant protection measures. The regulation creates a more efficient regulatory framework which enables multinational trials while maintaining safety standards and ethical requirements and scientific quality.

The Medical Device Regulation (MDR) (EU) 2017/745 functions as the fundamental regulatory system for medical devices entering the EU market. The Medical Devices Directive (93/42/EEC) and the Active Implantable Medical Devices Directive (90/385/EEC) received full implementation through MDR in May 2021. The new regulation establishes higher standards for clinical evaluation and post-market surveillance and risk classification requirements. The regulation demands Unique Device Identification (UDI) for traceability purposes and enhances the oversight responsibilities of notified bodies. The regulation provides enhanced transparency through EUDAMED database access while requiring manufacturers to show safety and performance through comprehensive clinical and technical evidence. The MDR establishes requirements to maintain high quality and safety standards for medical devices from production through their entire life cycle.

1.2.Telemedicine in otorhinolaryngology

The field of otorhinolaryngology has increasingly adopted video-otoscopic methods which provide remote ear pathology diagnostic capabilities. ENT professionals use otoscopy as their essential diagnostic tool for checking ear canal conditions along with tympanic membrane status and otitis media infections within the middle ear. Digital otoscopy systems combined with smartphone-connected otoscopes and dedicated video-otoscopic devices let clinicians examine patients remotely through image transmission to make clinical decisions independently of physical interactions. Through video-otoscopy medical professionals can obtain high-quality images of the ear canal and tympanic membrane which they can send

asynchronously or utilize during live video consultations. The methods show particular value for medical assessments in rural areas as well as pediatric care and post-operative checks for tympanoplasty or tube insertion patients. The range of devices includes basic smartphone attachments together with professional digital otoscopes featuring integrated lighting and video recording functions.

Clinical trials that assess video-otoscopic methods encounter multiple challenges when evaluating their effectiveness and reliability. The quality of images in video-otoscopic assessments depends on both the used device and the operator's ability to position the camera correctly and achieve proper focus. The quality of images produced by non-specialist healthcare providers and patients remains suboptimal which reduces the accuracy of diagnostic results. Standardization between devices is absent which creates challenges when researchers want to evaluate study outcomes between different research settings or studies. The execution of trials faces multiple hurdles due to ethical and methodological challenges. The practice of remote diagnosis needs strict rules about when to refer patients to in-person exams and how to monitor their condition. The implementation of blinding techniques and control conditions becomes challenging for tele-otoscopy studies because it is challenging to compare remote otoscopy with traditional in-person examinations. The process of recruiting diverse participants faces difficulties because of both technological barriers and unequal access to healthcare. The main difficulty lies in meeting requirements for regulatory compliance together with data protection standards. The transmission of patient-identifiable visual data for video-otoscopic methods requires protection measures that follow GDPR and HIPAA regulations. The research needs to establish detailed informed consent procedures because image storage for delayed review and training dataset utilization requires special attention. Research findings show that remote otoscopic assessments share significant agreement with in-person examinations when evaluating conditions such as acute otitis media and cerumen impaction. Artificial intelligence-based image interpretation shows promise as an emerging field but researchers need to complete initial validation steps.

2. Aims

The main purpose of this research is to assess the clinical diagnostic and therapeutic accuracy of telemedicine software in relation to conventional standards through detailed statistical analysis of matching diagnoses and therapies in clinical data. The thesis also aims to examine the effects of regulatory frameworks on the development, approval and implementation of telemedical and medical technology products including medicinal products, standalone medical devices and combined drug–device products. The thesis aims to integrate clinical performance data with regulatory analysis to provide a comprehensive understanding of the challenges and opportunities associated with the clinical evaluation and market integration of telemedicine technologies, thus contributing to more effective and safer innovation in digital healthcare.

Main objectives:

1. To analyze how product classification influences clinical trial requirements and post-market obligations.
2. Comparing clinical trial methodologies and regulatory frameworks for medicinal products and medical devices.
3. To evaluate the diagnostic accuracy of a telemedical video-otoscopic device.
4. To assess the therapeutic alignment between the recommended diagnoses provided by the telemedicine system and the factual diagnosis.
5. To conduct cross-tabulation and overlapping analysis of diagnosis and therapy data to understand the clinical relevance of non-exact matches and explore possible patterns of partial concordance.

3. Methodology

3.1.Analysis and comparison of clinical trial routes based on product category

The methodology to evaluate drug and medical device clinical trial differences and similarities requires analyzing the governing regulations through a comparative study of EU Regulation (EU) No 536/2014 for drugs and EU Regulation (EU) 2017/745 for medical devices by examining trial design and approval processes and ethical over-sight and transparency requirements. The analysis relies on process mapping to show procedural steps and regulatory actors and selected case studies from public databases (e.g., EudraCT, EUDAMED) to identify practical differences in trial implementation. The analysis draws additional insights from academic literature and regulatory reports and stakeholder perspectives when possible. The analysis aims to reveal regulatory convergence areas while explaining sector-specific limitations and adaptable elements.

3.2.Evaluation of the performed telemedical clinical trial

3.2.1. Applied telemedicine device and software

The telemedicine software developed by the University of Szeged was used for the study, which supports the transmission and analysis of otoscopic images and clinical data. The device consisted of a CE-marked optical unit applied (Cupris TYM smartphone otoscope device, Cupris Ltd., Somerset, UK) to a CE-marked smartphone and the software that operates the system, and was the subject of the test, as well as a detailed user guide. The device was used to record videos of the external auditory canal and the tympanum, and to record clinical data (symptoms, complaints). The phone application transmitted the data to the examining physician, who analyzed the data, made a diagnosis and therapeutic recommendation and arranged the following visit.

3.2.2. Participants of the study

The study was conducted in accordance with the Declaration of Helsinki. It was approved by the Medical Research Council and the National Scientific and Ethical Committee (OGYÉI/1422/2020). Written informed consent was obtained from the patients or their parents/guardians before the study and participation was voluntary. The study included 103 patients aged 0–100 years with otorhinolaryngological complaints, and who have consented to the examinations. From January to May 2020, data were collected from patients with otorhinolaryngological complaints admitted at the Department of Oto-Rhino-Laryngology and

Head-Neck Surgery, Faculty of Medicine, University of Szeged, based on the inclusion and exclusion criteria. The patients with ear complaints (mainly but not limited to earache, discharge from the ear, itching, and cerumen accumulation) were involved in the study, who communicated well with the investigator and could understand and comply with the requirements of the protocol and signed the informed consent. The exclusion criterion of the study was, on the one hand, the patient's withdrawal of informed consent at any time after being informed and signing, thereby suspending his or her participation orally or in written form. On the other hand, patients with poor general conditions, traumatic events or symptoms that may be directly life-threatening were excluded from the study, as determined by the investigator (e.g., cerebrospinal fluid leakage or massive bleeding). Further exclusion reason was any medical condition which, in the investigator's opinion, may have compromised the patient's health and/or contraindicate the conducting of the study, or the patient's participation was suspended for any reason according to the investigator.

3.2.3. Study protocol

Patients who visited the Department of Oto-Rhino-Laryngology and Head-Neck Surgery or outpatient clinic were informed about the nature of the study before signing the informed consent forms. Then, the data necessary for the demographic data of recruited patients were recorded in the telemedicine software by a physician/nurse from primary care (who is not an otorhinolaryngologist specialist). After that, a static image or video (otoscopic recording) of the external auditory canal and the tympanum was recorded, uploaded into the telemedicine system and shared with a specialist (otorhinolaryngologist no. 1.) for selecting the proposed diagnosis in the telemedicine system based on the telemedicinal data. Parallel to that, the patient was physically examined by another independent specialist (otorhinolaryngologist no. 2.) who recorded the anamnesis with the same questions included in the telemedicine system, defined diagnosis, and recommended therapy from the optional list that was included in the telemedicine system. Finally, an individual expert (otorhinolaryngologist no. 3.) compared whether the diagnoses and the treatments made by the two methods were matching. In the case of the match, only one was assessed; however, if there was a difference, both were assessed.

3.2.4. Data analysis

The main aim of the study was to compare the consistency of the diagnoses and treatments made by remote diagnostics and on-site specialists. The primary target variable was the "ratio of matches", which defines the percentage result of matches compared to total number of cases.

Principally, the diagnosis was selected based on the International Statistical Classification of Diseases and Related Health Problems (ICD). The two study results are considered matching if the same diagnosis was selected from the drop-down menu and the main group (first level) of therapy was the same (not at the active pharmaceutical ingredient and dose level), and was confirmed by the independent expert. For demographic data evaluation, descriptive statistics provided the number of cases, the mean value, the standard deviation, the minimum, the median and the maximum values. In the category variables, the number of cases and the frequency of occurrence were given.

The primary efficacy analysis examined the ratio of the matching therapies and diagnoses. The ratios and the 95% confidence intervals are given, and the Wald test was used to study the matches above 90%. The statistical significance level was 0.05. The secondary efficacy analysis examined the ratio of matching therapies and matching diagnoses. The ratios and the 95% confidence intervals are given, and the Wald test was used to study the matches above 90%. The statistical significance level was 0.05. Descriptive statistical methods were applied for further analyses (same diagnosis, different therapy, matches per each optional diagnosis).

The ratio of different therapies and diagnoses and the ratio of matching and overlapping therapies and diagnoses were studied. These ratios and the 95% confidence intervals are provided.

4. Results

4.1.Comparative analysis of the EU clinical trials based on product category

Each approval process for medicinal drugs and medical devices and drug-device combination products has its own set of regulatory guidelines and clinical testing and post-market monitoring protocols. A study design should adapt to these differences because it needs to meet regulatory requirements to obtain market authorization. The paper investigates product-related clinical aspects alongside regulatory aspects of these products through an organized comparative analysis.

Medicinal products in the European Union fall under the Clinical Trials Regulation (CTR) No. 536/2014 which unifies clinical trial oversight throughout member states. The Clinical Trial Information System (CTIS) serves as a centralized system to handle applications and monitoring which provides unified regulatory and ethics committee evaluation across the EU. The Medical Device Regulation (MDR) 2017/745 oversees medical devices while emphasizing safety performance and post-market surveillance responsibilities. The MDR imposes distinct clinical trial obligations based on device risk categories from Class I to III. The regulatory evaluation of combination products becomes longer because these products must follow two different regulatory systems when their primary mode of action determines which authority leads the assessment process. The submission of Drug Clinical Trial Applications (CTAs) through CTIS requires unified regulatory and ethics committee clearance. The sponsors of medical devices need to submit clinical investigation applications to national authorities and ethics committees but face more detailed evaluation processes for Class III high-risk devices. The dual assessment process for combination products becomes more complex because regulators need to work together for coordinated submissions and reviews and this additional work increases administrative challenges.

The drug development process contains four sequential phases starting with Phase I safety evaluation in healthy volunteers followed by Phase II efficacy testing in small patient groups and then Phase III large-scale randomized controlled trials and Phase IV post-market surveillance. The development process for medical devices does not involve phased testing because these products need feasibility and pivotal studies that follow risk class guidelines. The assessment of drug efficacy and device performance needs to happen simultaneously during the trials of combination products. Medical studies employing drugs normally utilize randomized controlled trials with blinding and placebo controls but ethical considerations limit this

approach. Medical device trials require usability assessments as well as comparative studies that do not support the use of blinding or placebo because these methods are either impractical or unethical. The combination of drug and device evaluation methods in these trials creates complicated experimental designs that require larger participant numbers to evaluate complete safety and effectiveness.

The endpoints used in drug assessments consist of pharmacokinetics together with efficacy and safety metrics using standardized outcome measures but medical devices assess performance together with usability and procedural success. The analysis of combination products becomes more complicated because they need composite or dual primary endpoints which require additional statistical complexity. The review duration at the EMA ranges from 12 months to 18 months for new drugs yet it moves faster for low-risk devices and takes longer for Class III devices together with combination products because of dual regulatory oversight. The pharmacovigilance requirements for drugs include adverse drug reaction reporting while devices need tracking systems for technical failures and safety incidents. Both pharmacovigilance systems from drugs and devices need to operate together for combination product risk monitoring. The manufacturing requirements for drugs follow Good Manufacturing Practice (GMP) but devices must comply with ISO 13485 while combination products need to fulfill both standards which creates substantial challenges. The qualifications of investigators depend on the intervention risks involved; drug trials need physicians who hold licenses while device trials can use other healthcare providers for low-risk devices and combination product trials always need physicians.

4.2.Evaluation of the clinical trial on the video-otoscopic telemedical device

4.2.1. Demographic and basic characteristics

One hundred and three (103) patients were enrolled in the study: 54 females (52%) and 49 males (48%) with an average age of 45.5 ± 19.57 years (range, 15–96 years) with a median age of 43.5 years. The cohort was predominantly composed of adults, the median age was 43.5 years. Regarding the travel distance of the patients, we found that the involved patients traveled an average of 12.9 km between their residence and the clinic, most of them by car (31.1%). Moreover, due to the otorhinolaryngological examination, 39.8% of the patients had lost working hours, an average of 2.7 h (SD, 1.85). Telemedicine solutions offer a suitable alternative to reduce travel distance, time and costs, as well as the loss of working hours. Using a smartphone otoscope device, the patient or their relative was able to capture static images or

video from the affected ear canal at home easily and comfortably, and it provided for establishing a remote diagnosis to the healthcare specialist through the telemedicine software.

4.2.2. Number of matches in the diagnoses and therapies together

The matching of the diagnoses and therapies was investigated simultaneously during the primary analysis of the telemedicine software. However, full matches were only found in 56 of the 103 cases examined, and the rate of the matching cases was 54.4% (95% CI: 44.7–64.0%). The ratio of the matching cases was significantly lower than the expected 90% matching (Wald test, $p < 0.001$). Therefore, in the secondary analysis, the matching of the diagnoses and therapies was investigated separately to determine which case resulted in a more remarkable difference.

4.2.3. Number of matches in the diagnoses individually

During the secondary analysis of telemedicine software, the matching in diagnoses was first investigated. The results showed that matching diagnoses were found in 79 of the 103 investigated cases, and the rate of the matching cases was 76.7% (95% CI: 68.5–84.9%). The ratio of the matching cases was still significantly lower than the expected 90% matching (Wald test, $p < 0.001$). However, these results indicated that the telemedicine software is suitable for remote diagnostics. A higher number of cases may increase the rate of matching cases.

4.2.4. Number of matches in the therapies individually

In the other part of the secondary analysis, for the matching therapies, it was revealed that matching therapies were found in 61 of the 103 investigated cases; the rate of the matching cases was 59.2% (95% CI: 49.7–68.7%). The ratio of the matching cases was significantly lower than the expected 90% matching (Wald test, $p < 0.001$). This result indicates that the number of matchings in primary analysis was lower because of the relatively high number of failed matches in therapies.

4.2.5. Number of matches in the diagnoses in the case of different therapies

The following level of secondary analysis focused on the 79 patients who had their diagnoses verified to assess treatment decision agreement between accurate diagnoses. This evaluation analyzed the relationship between achieved diagnostic agreement and improved therapeutic choice consistency. 79 participants showed therapy matching in 56 cases (70.9%), but 23 patients (29.1%) received different therapy recommendations than the reference standard. The data reveals an important pattern because diagnostic alignment increased the

chances of therapy alignment, yet did not ensure complete alignment. The therapy recommendations for 30% of patients who received accurate telemedicine diagnoses did not match the reference standard, indicating a therapeutic-planning disconnect in telemedical workflows.

4.2.6. Matching by optional diagnosis

The secondary analysis reached its advanced stage to evaluate how well the software matched both diagnoses and therapies with the optional diagnoses it generated. The software generates optional diagnoses through algorithmic processing of otoscopic images and patient symptoms and structured input data. The analysis served two purposes: it evaluated the diagnostic reliability of the telemedicine tool for each disease category and it determined if accurate condition diagnosis led to equivalent accurate therapy recommendations. The detailed analysis reveals important information about how the software performs in treating different otologic pathologies.

The results are divided by diagnostic label to assess software performance at both the aggregate and individual disease condition levels. The evaluation of software performance requires condition-specific analysis because otologic pathologies present different levels of diagnostic and therapeutic complexity ranging from simple recognizable cases with standard treatment to complex cases needing individualized management.

The telemedicine system produced more optional diagnoses in conditions where Otitis externa (n = 30), Impacted cerumen (n = 26), Eustachian salpingitis (n = 12), and Otitis externa maligna (n = 5) appeared — and the diagnostic matching rate exceeded 75% with strong validity support. The diagnostic matching rate for Impacted cerumen reached 83.9% (95% CI: 68.2%–93.6%) and Otitis externa reached 78.9% (64.2%–89.5%) which indicates strong agreement between software assessments and the reference standard. The system demonstrates reliable diagnostic performance in detecting common conditions with distinct otoscopic features and minimal dependence on patient history or subjective symptoms.

The therapy matching rates for these conditions demonstrated lower and more inconsistent results compared to the diagnostic matching rates. The therapeutic agreement for Otitis externa reached 42.1% while Eustachian salpingitis showed a lower 43.8% agreement despite achieving a 75.0% diagnostic match rate. The study confirms previous research showing that diagnosis and therapy matching do not follow a direct linear relationship. The system demonstrates effective condition identification but fails to generate suitable treatment plans consistently

because its decision-support algorithms or contextual inputs are limited. The condition Impacted cerumen produced exceptional results because it achieved both high diagnostic (83.9%) and therapeutic (87.1%) match rates. The software demonstrates both diagnostic and therapeutic effectiveness when dealing with basic algorithmically simple conditions that have limited treatment choices such as ear irrigation and manual removal. The limited treatment options together with predictable clinical practices explain this consistent performance.

The analysis of diagnostic categories with small case numbers ($n < 5$) revealed large data variability which produced extensive confidence intervals for proportions. These findings must be interpreted with caution due to the limited statistical power. Acute tympanic membrane inflammation and Other otitis externa achieved perfect diagnostic and therapeutic agreement (100%) yet each result derived from one or two cases. Although the numbers seem impressive at first glance they do not provide generalizable results because they might represent statistical anomalies or selection biases. The unspecified Otitis media condition received a diagnostic match rate of 10.0% which stood as one of the lowest rates throughout the entire dataset and its corresponding therapy match rate reached 40.0%. The software demonstrates classification and treatment decision-making weaknesses in ambiguous cases that present either overlapping symptoms or indistinct otoscopic features. The diagnostic match rates for Acute serous otitis media and Chronic serous otitis media reached 36.4% and 0.0% respectively because fluid-based middle ear conditions present challenges to remote identification and treatment. The diagnosis of these conditions requires pneumatic otoscopy or tympanometry for proper assessment because these essential tools cannot be used in video-otoscopic telemedicine.

The diagnostic agreement for Sensorineural hearing loss reached 0.0% but the therapy matching rate reached 100%. The treatment decisions made for these cases either occurred incidentally or the standard treatment approaches were so common that they did not depend on accurate tele-diagnosis results. The lack of audiometric data in telemedicine settings makes it impossible to diagnose sensorineural pathology accurately because this explains the diagnostic failure. The diagnostic categories showed inconsistent results between their diagnostic agreement and therapy agreement levels. The unspecified Hearing loss diagnosis received a 50.0% diagnostic agreement rate which correlated with an 83.3% therapy match rate indicating that although diagnostic specificity was weak the treatments followed standard care protocols.

5. Discussions

5.1.Comparison and analysis of clinical trials based on product category

Research development along with regulatory planning requires correct medical product classification into medicinal drugs and medical devices and combined drug-device products. All stages of regulatory procedures along with clinical trial design and risk evaluation and manufacturing standards and post-market responsibilities get their direction from classification. The importance of accurate classification continues to rise with increasing adoption of therapies that integrate multiple functions The Clinical Trials Regulation controls the systematic clinical trial process which consists of four phases (I–IV) that test pharmacokinetics and assess efficacy and safety. Medical trials need big participant numbers along with randomization and placebo controls and must follow extensive post-market surveillance procedures. Medical devices classified into Classes I to III undergo testing methods that analyze usability and mechanical performance alongside local body interactions using smaller participant samples.

The regulatory requirements for combined drug-device products including autoinjectors and drug-eluting stents depend on their primary therapeutic purpose between medicinal and device regulations. The dual regulatory requirements of these products demand manufacturers to meet GMP and ISO 13485 standards and to conduct clinical assessments that measure drug effectiveness and device operational capability. Early development misclassification results in substantial delays because regulatory submissions fail or clinical trials prove incompatible. The design of clinical trials for hybrids requires expanded participant numbers and dual-endpoint assessment to properly measure both system components. The duration of regulatory review differs because drug approvals need lengthy safety and efficacy assessments while device approvals proceed faster except for Class III devices but combined products experience the longest review duration because of dual assessment requirements. The dual nature of combined products leads to separate monitoring systems for drugs to track adverse reactions and devices to detect technical failures alongside user errors. The integration of multiple monitoring systems by combined product manufacturers elevates their quality management challenges.

Drugs need to follow GMP guidelines but medical devices need ISO 13485 certification. The development of combined products needs multiple professionals including engineers together with pharmacists and clinicians and regulatory specialists to fulfill both standards. The entire development lifecycle receives its direction from product classification because it determines both regulatory clarity and trial efficiency and approval speed and patient safety.

The correct initial classification serves as a vital requirement for achieving innovation and compliance along with commercial success in modern healthcare systems.

5.2.Evaluation of the performance of the oto-videoscopic telemedical device

The clinical evaluation of a telemedical oto-videoscopic device revealed both positive aspects and negative aspects in this thesis. The diagnostic agreement rate reached 76.7%, which indicates promising potential for remote diagnostics, yet falls short of the desired 90% concordance benchmark. The therapy matching results were lower at 59.2% because remote diagnosis translation into suitable treatment decisions proved challenging.

The telemedicine decision-support tools require improvement because 70.9% of cases with matching diagnoses received matching therapies, but 29.1% received non-matching treatments. The diagnostic and therapy match rates were higher for common conditions such as impacted cerumen and otitis externa, but rare conditions demonstrated lower agreement, which indicates the need for advanced algorithms or expert hybrid systems to handle complex cases. The diagnostic and therapeutic matches combined or overlapped in 86.4% of cases which demonstrates substantial clinical value beyond the requirement of exact matches. The clinical utility of diagnoses and therapies exceeded 88% in non-matching cases and reached 94% for therapies. Telemedicine assessments provide useful support to clinical practice even though they face challenges from incomplete or secondary data that occurs during remote examination settings.

5.3. Application of telemedicine in otorhinolaryngology

Telemedicine has rapidly expanded across all ENT sub-specialties, enabling remote assessment, diagnosis, monitoring, and treatment. Virtual consultations facilitate outpatient management of conditions such as allergic rhinitis, sinusitis, laryngitis, and benign growth follow-ups. Patients can report symptoms and share images or videos, allowing clinicians to triage cases and identify those needing urgent in-person evaluation, such as new hoarseness requiring laryngoscopy.

6. Conclusion

The research explored clinical evaluation procedures across different medical products through an evaluation of telemedicine technologies together with drug and medical device and combined drug-device regulatory requirements. The regulatory framework analysis demonstrated that clinical trial methods for product categories vary through their framework rules and trial methodologies and risk assessments and approval processes. The distinction between clinical and regulatory approaches is essential for medical innovation today because hybrid therapies and integrated devices breach traditional rules.

Medical products require strict multi-stage trials with specific phases to test pharmacokinetics and safety and efficacy through extensive patient populations with controlled placebo-based studies. The risk classification system for medical devices supports adaptable clinical trials which evaluate performance and usability and device safety. The regulatory oversight for combined drug-device products creates extended difficulties in trial execution as well as manufacturing requirements and post-market monitoring procedures. The correct identification of product type during development ensures both simpler regulatory approval procedures and better clinical trial design and improved patient protection.

The telemedicine clinical study evaluated the clinical validity of a video-otoscopic telemedical device by examining its real-world applicability in medical practice. The study revealed a diagnostic agreement rate of 76.7% that demonstrates strong potential of the telemedicine system for remote otorhinolaryngology diagnosis. The study results indicated that therapy matching was lower at 59.2% because remote care settings presented difficulties in aligning diagnostic outputs with treatment choices. The research demonstrated that common medical diagnoses achieved better agreement levels yet rare and intricate cases created measurement fluctuations which required ongoing development of telemedical decision-support systems.

This thesis combines regulatory aspects with clinical trial data analysis to present a complete overview of medical product development and telemedicine implementation. The thesis demonstrates that healthcare innovation requires both technological advancement alongside strict clinical validation and regulatory clarity. Telemedicine expansion requires understanding its clinical performance and regulatory standards to create safe and accessible healthcare solutions that work effectively.