Implementing Horizon Scanning as a Tool for the Strategic Development of Regulatory Guidelines for Nanotechnology-Enabled Health Products

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INTRODUCTION

The global nanotechnology market, particularly nanotechnology-enabled health products (NHPs), is seeing significant growth (1). Yet, a gap exists between research and marketable products due to slow regulatory advancement (2). Horizon Scanning, a tool used by policy makers worldwide, identifies significant developments and threats and could be key in supporting to bridge this gap (3-6). Implemented through exploratory or issue-centered scanning, Horizon Scanning focuses on short to medium term topics rather than broad predictions. Regulatory agencies use it to identify future needs and establish guidelines, streamlining the path to market for innovative products. In this work we implemented Horizon Scanning methodology for NHP advancements, predicting trends and enhancing regulatory guidelines' strategic development.

MATERIALS AND METHODS

Regulatory database

A regulatory database was gathered, including guidelines and documents related to nanotechnology-enabled health products (NHPs) up to August 31st, 2023. Sources included competent authorities like EMA and FDA, European Commission, OECD, and standard-emitting organizations like ISO and ASTM.

Horizon Scanning methodology

This research applies the Horizon Scanning methodology in four stages based on the exploratory scanning approach (including signal detection, filtration, prioritization, and assessment). Signal detection uses various sources such as scientific publication databases and international patent registries, with searches conducted over distinct periods from January 2020 to June 2022. Irrelevant results were discarded. Filtration and prioritization utilized novelty as a criterion to eliminate irrelevant signals and categorize results into potential trends or disruptive elements, based on metrics proposed by Shah et al., 2003. This approach measures novelty by comparing how unusual an idea is relative to others. Finally, an assessment was carried out on the detected trends for their potential impact on the current regulatory state-of-the-art. This analysis aimed to identify how these signals fit within the existing regulatory science and potential areas of insufficient regulation.

Classification system for nanotechnology-enabled health products

Detected signals on NHP development have been indexed following the classification system described in a previous work of our group (7). This classification system considers both scientific and regulatory criteria and allows the grouping of NHPs into different categories, expected to share similar relevant characteristics when evaluated by regulatory authorities (refer to Figure 1). The system assigns a unique four-digit code, or classification signature, to each category of NHP. This code is based on the NHP's principal mode of action, chemical composition, intended purpose, and the approach followed in its nanofabrication (7).

RESULTS AND DISCUSSION

Signal detection for Horizon Scanning implementation involved databases that represent NHPs at various stages. Scopus, the European Patent Office (EPO) Database, and ClinicalTrials.gov were used for signal detection. These databases cover NHPs in early stages and also those assessed by a regulatory authority (either products preliminary assessed before a clinical study is initiated or product that already available in the market).

For filtration and prioritization of detected signals, novelty was used as a key criterion. A novelty quantification methodology was applied, which assigned higher novelty scores to the typology of NHPs less repeated within the whole distribution (Figure 2).

The results show a clear trend towards the development of drug delivery systems (DDS) and a growing trend in the development of nanomaterials for dental applications. Furthermore, the most disruptive elements involve NHPs that are multicomposite and multifunctional, harnessing nano-scale properties to combine therapeutic and diagnostic purposes within a single product. When compared with the regulatory landscape, current regulations are gradually adapting to accommodate emerging trends, with specific guidelines being developed. However, for the most disruptive elements, multicomposite and multifunctional NHPs, their novelty still poses significant regulatory challenges, requiring a strategic development of guidelines by regulatory agencies to ensure their safe and effective integration into healthcare practices. This study underscores the importance of proactive regulatory planning to bridge the gap between NHP innovation and market implementation.

In conclusion, there is a disparity between the innovative NHPs being developed and those that achieve regulatory approval. This is primarily due to

the lack of adequate regulatory guidelines. The application of Horizon Scanning methodology can be key for anticipating future regulatory needs. This study identifies DDSs and dental applications as leading trends in NHP development, and multifunctional and multicomposite products identified as the most novel. The continued focus on developing robust and adaptable regulatory guidelines for these types of NHPs is of utmost importance.

References

1. Bosetti R, Jones SL. Cost-effectiveness of nanomedicine: estimating the real size of nano-costs. Nanomedicine (London, England). 2019;14(11):1367-70.
2. Ali F, Neha K, Parveen S. Current regulatory landscape of nanomaterials and nanomedicines: A global perspective. Journal of Drug Delivery Science and Technology. 2023;80:104118.
3. Delaney K. INNOVATION TOOL KIT – Horizon Scanning. 2014.
4. Shimokawa M, Sato D, Wakao R, Arai H. PMDA's Vision for Horizon Scanning of Emerging Technologies Potentially Relevant to the Development of New Medical Products: The Regulatory Challenge. Clinical pharmacology and therapeutics. 2021;109(2):295-8.
5. Fukaya-Shiba A, Shimokawa M, Sasaki H, Wakao R. Pharmaceuticals and Medical Devices Agency's horizon scanning and the Science Board: Cooperation toward extracellular vesicle-based products. British journal of clinical pharmacology. 2022;88(3):1392-4.
6. Vignali V, Hines PA, Cruz AG, Ziętek B, Herold R. Health horizons: Future trends and technologies from the European Medicines Agency's horizon scanning collaborations. Frontiers in Medicine. 2022;9.
7. Rodríguez-Gómez FD, Penon O, Monferrer D, Rivera-Gil P. Classification system for nanotechnology-enabled health products with both scientific and regulatory application. Frontiers in Medicine. 2023;10.

Figures

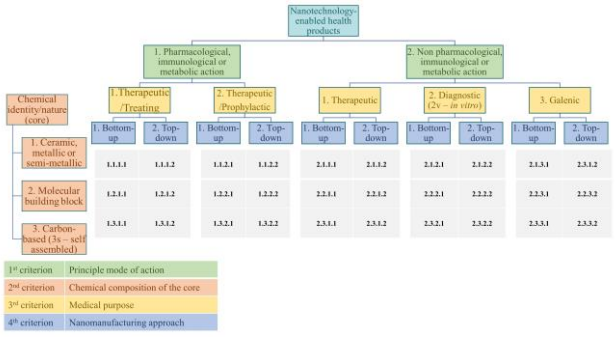

Figure 1. Nanotechnology-enabled health products classification system (taken from Rodríguez-Gómez *et al.*, 2023).

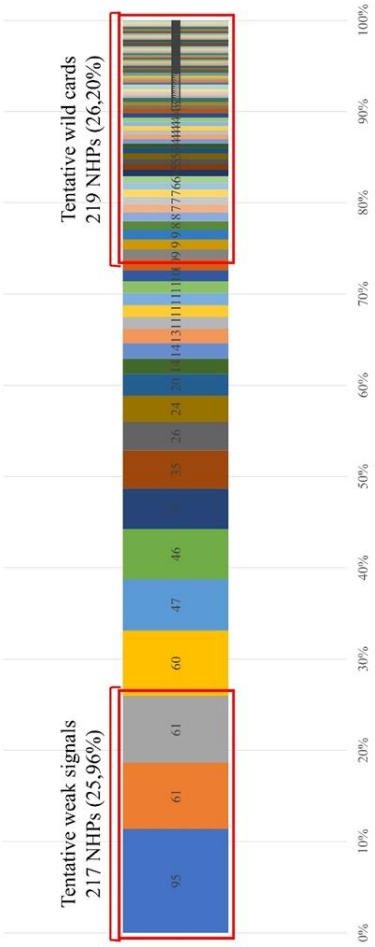

Figure 2. Cumulative percentage of the frequency of design solutions. Novelty analysis of the design solutions of detected signals. Design solutions are in descending order of frequency (i.e., in ascending order of novelty). The red squares show the 0.25 and 0.75 percentiles, Q1 and Q3, respectively. All design solutions with a frequency higher or equal to Q1 are considered tentative trends, all design solutions with a frequency lower or equal to Q3 are considered tentative wild cards.