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Future Nanomedicines: building a regulatory framework for the first-in-human nanoswarm cancer clinical trial

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This paper will provide an overview of future nanomedicines and focus on what is needed to build regulations for nanoswarms in clinical trials in the UK, Europe and the US. As and when this technology becomes ready for first-in-human tests, decisions will have to made about how it can and should be safely tested.

Overview: Cancer nanomedicine

Cancer nanomedicines can be used as drug carriers that can target tumours more effectively with anti-cancer agents, while leaving normal tissues untouched. Swarm behaviour, present in social animals such as birds, ants, fish and termites, can be designed using a systems approach as *in silico* modelling is an effective tool that can minimise costly trial-and-error methods[1, 2]. Researchers can use simulations for selecting nanoparticles so drugs can more effectively reach the tumour while avoiding side effects. Advancements in nanomaterial-based approaches and artificial intelligence (AI) offer unique opportunities for researchers to go beyond nanoparticle selection. Researchers are investigating controlling the movement of nanoparticles to establish an intelligent drug delivery system. These intelligent nanoparticles or nanorobots are nano-sized entities that can control their motion and interactions with the environments[3]. Nanoswarms are multiple nanoparticles or nanorobots that can interact with each other or their environment to achieve a task (e.g. deliver chemotherapy to a tumour without killing healthy cells), exhibiting collective behaviour inspired by swarms[1, 2, 4].

Commentary: Nanoswarm classification

The classification of nanoswarms as a drug delivery system is likely to fall under the medical device category, however, this will be dependent on the application and each country's regulatory body. Medical device and drug trials have very different requirements in most countries. There is the added complexity of different regulations for software as a medical device and other guiding AI principles. Policymakers need to co-design regulations with developers, patients, healthcare workers and the public as this will be essential for innovation, development and to reap the benefits of nanoswarm technology. Nanoswarms do not generate entirely new categories of ethical issues, but they do require us to think carefully about whether our current theories and approaches can provide the guidance we need. A concern amongst researchers is that overly restrictive legislation, arising from ethical concerns, will stifle research at a time when it is increasingly needed as cancer incidence rises[3]. Additionally, nanomedicines could increase the divide between high- and middle- or low-income countries, leading to a so-called 'nano-divide'[3]. It also seems clear that nanoswarms could in principle be deployed to harm, as well as heal. This 'dual use' problem is not unique to this technology and cannot be managed by regulators alone; additional legal mechanisms must be in place.

Conclusion: Regulating the next frontier of nanomedicines

Nanotechnologies have been used in the clinic for years. For all their potential medical applications, nanoswarms are still largely in the research and development stage. The next frontier of nanomedicines in clinical trials have yet to be approved[3], but we ought to start thinking about what the first-in-human clinical trials of nanoswarms could or should look like, and ask how we will regulate the development of this new medical technology, in order to anticipate ethical controversies that may arise, and to mitigate risk[3]. We need to go beyond the usual process and

discuss everything from concept, design, testing, and mode and mechanism of action, to manufacturing and waste disposal and management. To aid clinical adoption of nanoswarms, a harmonised nanomedicine vocabulary is essential, and this is a pre-requisite for an effective regulatory framework[3]. We suggest, for now, that there are 6 central domains that need to be explored in order to draft guidance for regulation in this area, these are stakeholders, social/economical, in silico, *in vitro* and *in vivo* analysis, nanomaterials, legal, and approval process[3].

References

1. N. R. Stillman, M. Kovacevic, I. Balaz, and S. Hauert, “In silico modelling of cancer nanomedicine, across scales and transport barriers,” npj Computational Materials 2020 6:1, vol. 6, no. 1, pp. 1–10, Jul. 2020, doi: 10.1038/s41524-020-00366-8.
2. N. R. Stillman et al., “Evolutionary computational platform for the automatic discovery of nanocarriers for cancer treatment,” NPJ Comput Mater, vol. 7, no. 1, p. 150, Sep. 2021, doi: 10.1038/S41524-021-00614-5.
3. M. Swana, J. Blee, N. Stillman, J. Ives, and S. Hauert, “Swarms: The next frontier for cancer nanomedicine,” in Cancer, Complexity, Computation., 1st ed., vol. 46, I. Balaz and A. Adamatzky, Eds. Emergence, Complexity, Computation Vol 46. : Springer, 2022.
4. S. Hauert and S. N. Bhatia, “Mechanisms of cooperation in cancer nanomedicine: towards systems nanotechnology,” Trends Biotechnol, vol. 32, no. 9, pp. 448–455, Sep. 2014, doi: 10.1016/J.TIBTECH.2014.06.010.

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