Roundtable Session 2 – Table 6 – Point-of-Care Advanced Therapies in the Era of Decentralized Manufacturing

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Abstract:

Advanced therapy medicinal products (ATMPs), including cell and gene therapies, are driving a paradigm shift from centralized manufacturing models toward decentralized and point-of-care (PoC) production approaches. While PoC models may improve patient access and reduce treatment timelines, they also present challenges related to product quality, process consistency, regulatory oversight, and data integrity.
This roundtable will explore the opportunities and challenges associated with decentralized manufacturing of advanced therapies. Topics will include regulatory expectations, comparability across manufacturing sites, quality system requirements, digital and automated solutions, and strategies to ensure consistent product quality, safety, and efficacy.

Discussion Questions:

1. What are the greatest opportunities and risks associated with point-of-care manufacturing of ATMPs compared with centralized manufacturing models?

2. What evidence is needed to demonstrate comparability when introducing a new manufacturing site into an established point-of-care network?

3. How should regulatory frameworks evolve to adequately oversee point-of-care manufacturing while maintaining flexibility for innovation and timely patient access to advanced therapies?

4. What role will automation, digital batch records, remote oversight, artificial intelligence, and real-time analytics play in enabling scalable and compliant decentralized manufacturing networks?

5. At what point does a hospital operating a point-of-care manufacturing platform effectively become a pharmaceutical manufacturer, and what responsibilities, liabilities, and regulatory obligations should accompany that transition?

Notes:

Application and scope of decentralised manufacturing

- A distinction is needed between point-of-care (PoC) manufacturing and decentralised manufacturing (DM).
- The need for DM should be established first. Participants questioned who is asking for it and suggested it may be most appropriate only when absolutely necessary.
- Potential drivers include pressure from patients, families, hospitals and foundations, together with a desire to make treatment available on demand in a nearby hospital.
- Short shelf-life products, ultra-rare diseases and highly personalised medicines were identified as possible use cases.
- Some individualised therapies may benefit more from centralised manufacture, depending on process complexity and expertise requirements.

Potential manufacturing models and therapy fit

- A mobile, closed manufacturing unit or "box" located in a hospital was proposed. Inspectors would need to recognise and assess the system as closed.
- A hybrid model could retain centralised manufacture of drug substance (DS), with final formulation undertaken at the hospital.
- DM may be feasible for CAR-T therapies.
- Hospital-based PoC manufacture may be commercially viable for certain highly personalised products.
- Personalised gene editing may be less suitable for hospital-based PoC manufacture because it is highly manual and requires substantial expertise.
- Current hospital facilities may be better suited to early clinical trials than commercial manufacture; participants questioned whether existing infrastructure can transition to a commercial operating model.

Hospital capacity and operation burden

- Different developers use different processes, strategies and products, creating a significant burden for hospital units.
- Hospitals may require substantial additional trained personnel to operate multiple developer-specific processes.
- Participants questioned whether developers could allow hospitals greater control over processes such as apheresis.
- It is unclear whether hospitals would be willing to act as manufacturing spokes for multiple developers while maintaining their own clinical work.

- Capacity constraints require contingency planning: if one hospital has a patient but no capacity, could another hospital manufacture for that patient, and would this still qualify as PoC manufacture?
- Some hospitals may not fully recognise the limits of their authority or the responsibilities associated with pharmaceutical manufacture.

Good Manufacturing Practice and quality oversight

- Regulators were said to expect hospital manufacture to comply with Good Manufacturing Practice (GMP).
- Further regulatory discussion is needed to determine which steps must meet GMP requirements, particularly where a step does not involve the medicinal product or starting material.
- Controls and security must remain sufficient to demonstrate product safety.
- Participants asked whether the quality and evidence threshold for DM products should differ from centralised manufacture. The prevailing view was that patients face the same risks and that the same risk-based principles should apply.
- Ongoing obligations would include maintenance of standard operating procedures (SOPs) and preparation of annual reports.

Accountability and Qualified Person oversight

- Participants questioned whether a Qualified Person (QP) would be willing to assume responsibility for an entire decentralised network.
- Questions were raised about whether pharmacists could undertake the required work and where professional accountability would sit.
- A hospital moving into commercial production may effectively become a pharmaceutical manufacturer, with corresponding responsibilities and liabilities.

Ethical and regulatory issues for individual patients

- “Specials” and individual-patient manufacture raise ethical concerns where manufacture and release may occur with limited regulatory involvement.
- For an individual patient (n=1), treatment decisions may rest largely with the physician.
- For personalised therapies for ultra-rare diseases, there may be pressure to omit development steps because patients have very limited time.
- A regulatory-approved platform approach was suggested as a possible way to support such therapies.

Commercial viability, cost and reimbursement

- Participants questioned the underlying business model and the true cost of goods (COG).
- DM may cost more than centralised manufacture and was not viewed by all developers as cost-effective.
- DM may nevertheless attract incentives or be justified where unique eligibility criteria or clinical needs apply.
- Transparency about margins could be challenging. High margins may also fund other products in a development pipeline, raising the question of whether companies have a duty to disclose or explain them.
- Hospitals may charge substantial amounts for complex, expertise-intensive manufacturing activities.
- Reimbursement remains unresolved for personalised ultra-rare disease therapies.

Patient access considerations

- Decentralised approaches could reduce the need for patients to travel and may support patients who are unable to travel.
- Access benefits must be balanced against manufacturing complexity, capacity, cost and consistent regulatory control.

Regulatory development and next steps

- The manufacturing model and practical operating experience need to be developed before all regulatory questions can be resolved.
- Legislation may be designed to be future-proof, while detailed guidance may need to evolve as technologies and operating models become clearer.
- Policy, guidance, infrastructure and implementation should progress in parallel.
- Practical implementation is needed to reveal unforeseen issues and inform future requirements.
- Participants mentioned that the EMA have published a question-and-answer document on DM.