THE HURDLES TO MARKET – REGULATORY AND CLINICAL TRIAL CONSIDERATIONS IN EUROPE

Heike Schön, Managing Director

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WHO ARE WE?

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Heike Schön, Managing Director – an experienced and renowned consultant in preparing, setting up and overseeing clinical trials from both the sponsor's and the vendor`s side.

Liam Spencer, Senior Regulatory Project Manager - experienced in regulatory affairs having worked across a range of therapeutic areas, product types, and development phases

WHO ARE LUMIS?

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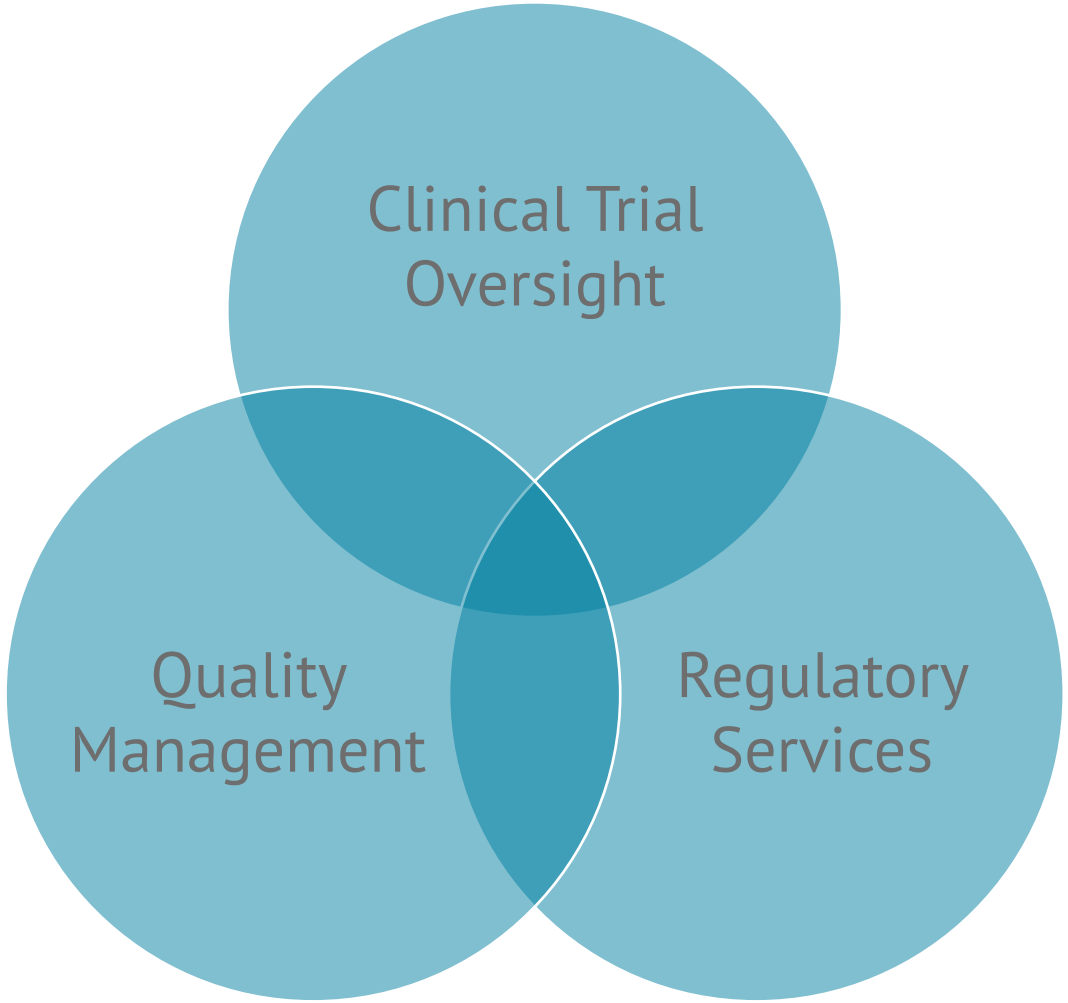
Who are Lumis Life Science Consulting?

We optimise pharmaceutical and medical device development via our solutions in clinical trials, quality management, and regulatory.

- Small consultancy
- Berlin HQ
- Range of pharmaceutical and medical device clients
- Particular interest in medicinal cannabis



AGENDA

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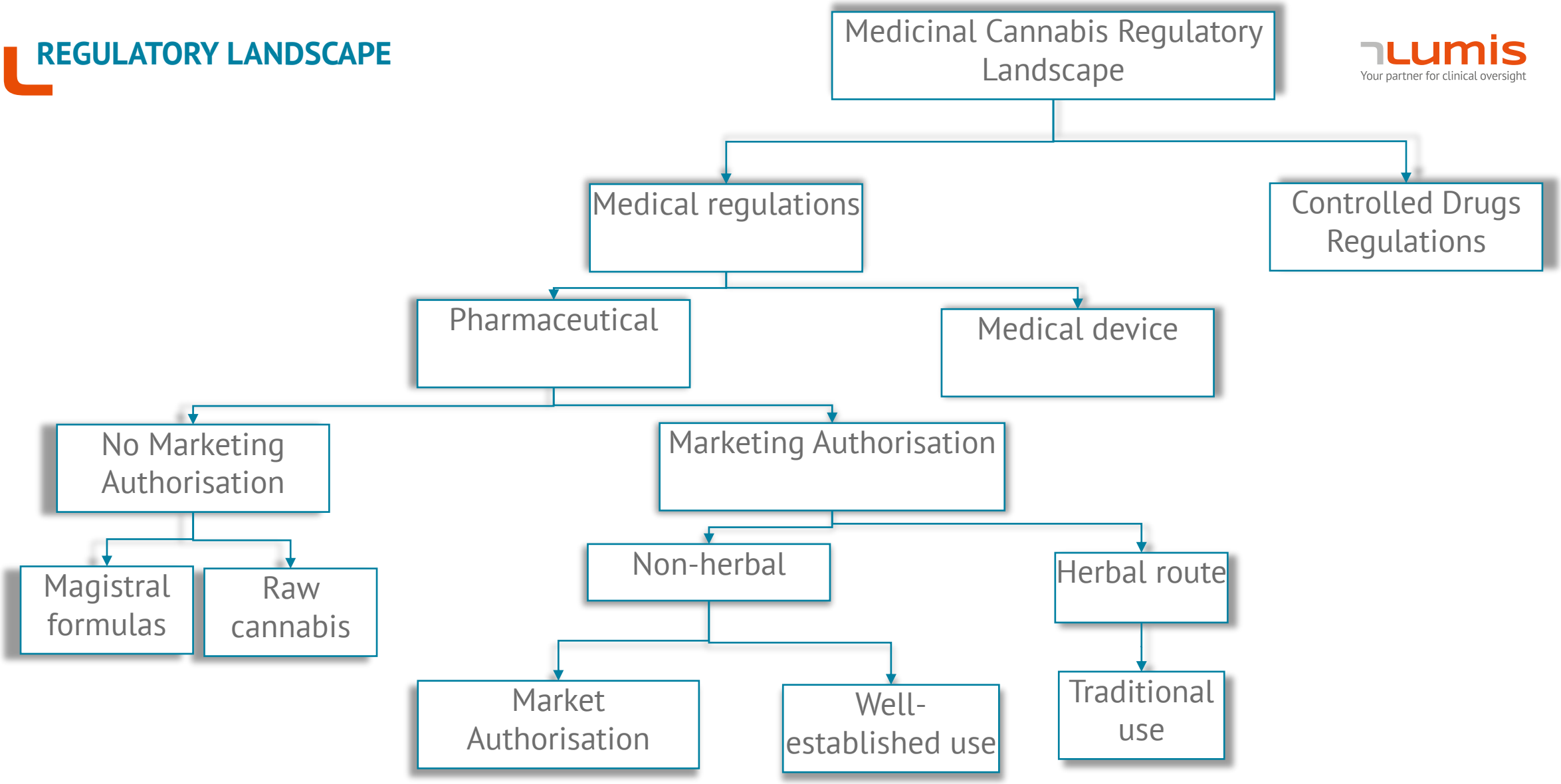
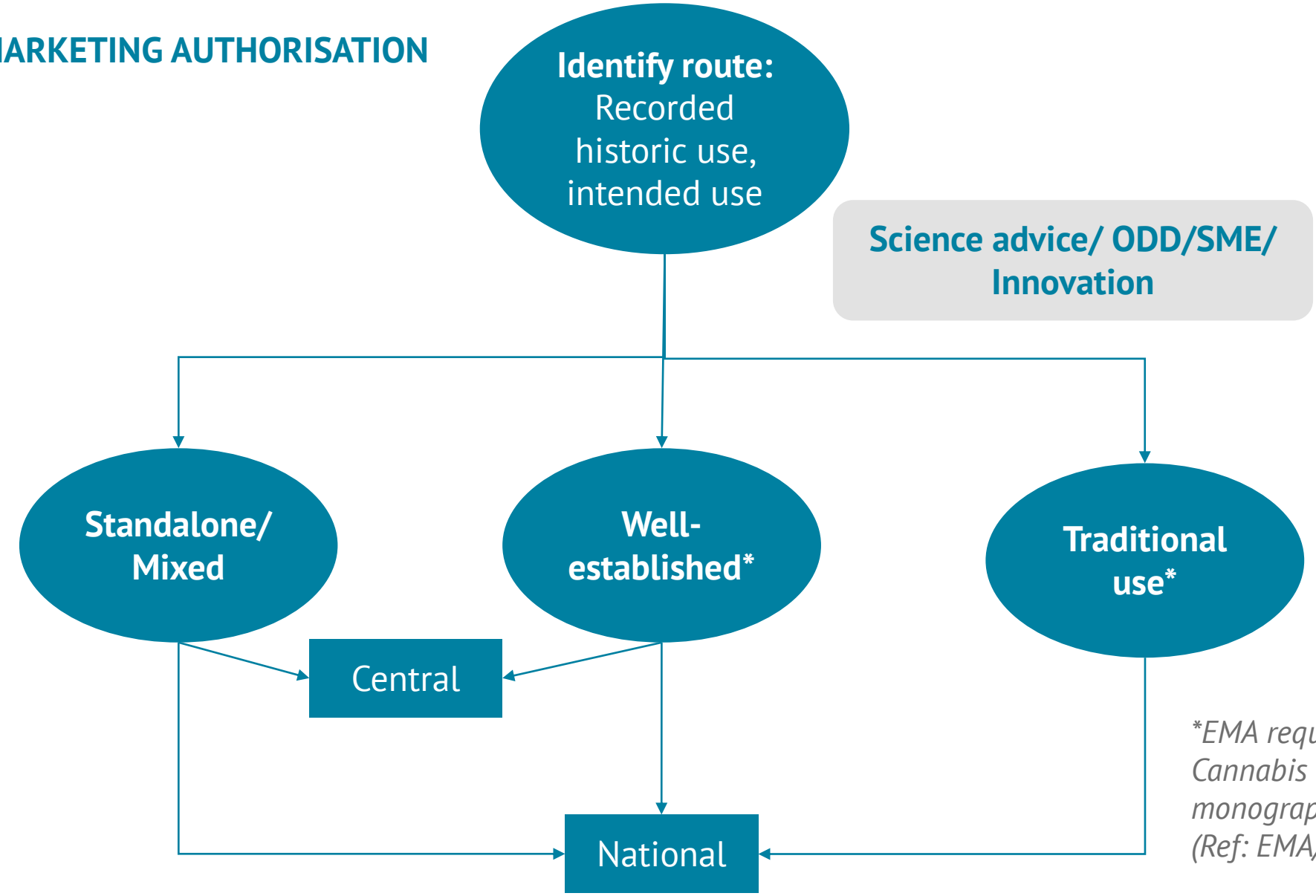
1. Introduction
2. Regulatory landscape
3. Clinical trial considerations
4. Conclusion
5. Further information
6. References

REGULATORY LANDSCAPE

REGULATORY LANDSCAPE



MARKETING AUTHORISATION



**EMA requested scientific data for Cannabis sativa L., flos – possible herbal monograph or list entry (Ref: EMA/HMPC/697513/2022)*

ADVANTAGE OF ORPHAN DRUG DESIGNATION (ODD) AND SME's Status

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- ✓ Financial advantages through fee reduction for regulatory activities
- ✓ 10 years market exclusivity for orphan drugs plus 2 years if paediatric investigational plan was executed
- ✓ Fast track appoval
- ✓ Support by EMA through protocol assistance
- ✓ Application for scientific advice can be done in parallel with US FDA
- ✓ Designated ophan medicines can apply for central marketing authorization
- ✓ If SME status is available company can obtain further full or partial fee exemptions

SMEs developed nearly 20% of human medicines recommended for authorization in 2020
of which 50% targeted a rare disease (EMA SME office)

NO MARKET AUTHORISATION

- Magistral/ officinal preparations (Article 3 Directive 2001/20/EC) or Specialities (Article 5 Directive 2001/20/EC)
- **Limited:** Individual patient, prescription only (sometimes specialist physicians only), physician's liability, lack of evidence, reimbursement, indications can be limited, cannabis sourced at state-level
- Examples – Germany, Netherlands, France, Ireland, Denmark, etc.

Legalised medicinal cannabis in 2017

Any doctor can prescribe,

Generally, for severe conditions with no alternative therapy

Any doctor can prescribe

Any justifiable indication

Inflorescence only

No clear medicinal cannabis program

MEDICAL DEVICE REGULATIONS

- Devices that administer a medicinal product fall under MDR 2017/745 (Article 1 (9))
- Integral vs non-integral
- Classification rules
- Medical device requirements: General Safety and Performance Requirements (GSPR), conformity assessment, CE marking (possibly)

DRUG CONTROL REGULATIONS

- Three UN Conventions (1961, 1971, 1988) outline drug controls
- UN conventions limit controlled drugs to ‘medical and scientific purposes’
- THC Content (varies by member state 0.2%-1.0%)
- Regulated at the member state
  - France – ANSM special authorisation permit for narcotic medicines
  - Ireland – Import permit applications require an annual licence and products to be included in Schedule 1 of the Irish Misuse Drugs legislation

CLINICAL TRIALS CONSIDERATIONS

MARKET SITUATION

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Sales in medicinal cannabis is estimated to grow to **58 Billion EUR** in 2028 (Bloomberg)

Unmet demand of medicinal cannabis products

Absence of significant clinical studies

Absence of scientific evidence on effectiveness of medicinal cannabis

Lack of harmonization and regulatory certainty

EU wide **centralized marketing authorization** is most beneficial to enable products to be marketed in whole EEA (e.g. Epidyolex from GW Pharma)

Preferred route for central marketing authorization through **Orphan Drug Designation**

REQUIREMENTS FOR CLINICAL TRIALS

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Design

Protocol, randomized CT (e.g.placebo controlled)

Primary and secondary variable

Clear inclusion and exclusion criteria

Quality of Life criteria

Safety measurements

Statistical evaluation

Conformity with applicable regulations to obtain regulatory and ethic committee approvals

Role of Sponsor company

All activities to conduct the CT can be delegated

Has to prove compliance with the applicable regulations through SOPs and implemented measurements

If non-EU company, need to assign legal representative

Sponsor has overall and final responsibility

Tools to be used

Oversight management to be implemented

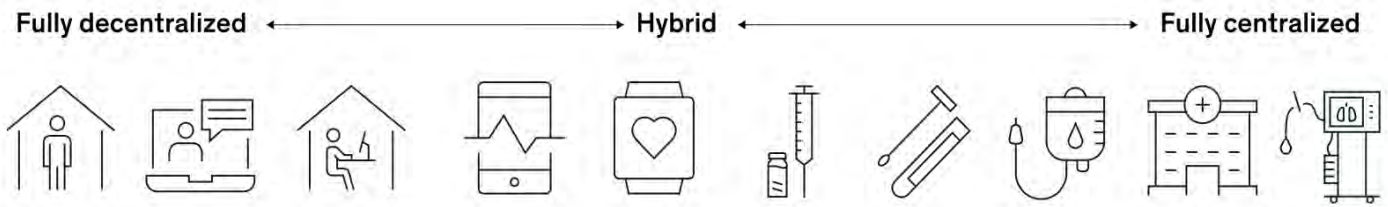
Key performance indicators to oversee quality, budget and timelines

Well defined contracts with vendors and their deliverables

Risk management plan

Decentralized clinical trials meet patients where they are.

Clinical-trial designs



All trial procedures are conducted virtually, enabled by digital technologies and supply delivery	Less complex trial procedures that don't require in-person visits (eg, vital signs, electrocardiograms) are conducted via telehealthcare, remote data collection, or direct-to-patient supply	Less complex trial procedures that require in-person visits (eg, injections) are conducted via mobile clinicians or alternative sites (eg, mobile clinics, retail sites)	Complex trial procedures (eg, complex screening protocols, cell therapy, magnetic resonance imaging) are conducted via research sites (eg, academic medical centers) or local hospitals	All trial procedures are conducted at a research site (eg, academic medical center)

McKinsey & Company

McKinsey & Company, June 2021
No place like home? Stepping up the Decentralization of clinical trials

USE OF TECHNOLOGIES IN DCTS SUPPORTING PARTICIPANT-CENTRIC APPROACH

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- eConsent
- eCOA (Clinical Outcome Assessment)
- eDiary
- Wearable/ sensors/smart watches
- Telehealth visits
- Local laboratory collections
- Mobile Health Apps
- Home healthcare visits
- Online survey
- ....

CONCLUSION

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Comment	*Lumis' advice*
Complex – Medicinal cannabis products can intersect multiple regulations at the EU and member state level	**Early planning –** Consider *all* applicable regulations as early as possible. **Scientific advice** can help ensure your plan is appropriate.
Development – medicinal cannabis development varies by product but a full quality module is always required	When possible, utilise regulatory incentives such as **Orphan Designation** and **SME status**
Clinical trial hurdles – one of the main hurdles for cannabis clinical trials is the cost for high quality studies	**Decentralisation/ hybrid –** Due to medical cannabis patients being largely outpatients decentralised/ hybrid designs could be beneficial

REFERENCES

1. EMA Market Authorisation Routes – Volume 2A Procedures for Marketing Authorisations, Chapter 1 – Marketing Authorisation, July 2019. https://health.ec.europa.eu/system/files/2019-07/vol2a_chap1_en_0.pdf
2. EMA Herbal Medicinal Products. https://www.ema.europa.eu/en/human-regulatory/herbal-medicinal-products
3. Questions & Answers regarding Cannabis-derived medicinal products1 and the scope of EU herbal monographs for herbal medicinal products within the EU medicines legislation. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/questions-answers-regarding-cannabis-derived-medicinal-products-scope-eu-herbal-monographs-herbal_en.pdf
4. European Union Monographs and List Entries. https://www.ema.europa.eu/en/human-regulatory/herbal-products/european-union-monographs-list-entries
5. Guideline on non-clinical documentation in applications for marketing authorisation/registration of well established and traditional herbal medicinal products. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-non-clinical-documentation-applications-marketing-authorisation/registration-well-established-traditional-herbal-medicinal-products-revision-1_en.pdf
6. Herbal medicines: regulatory and scientific support https://www.ema.europa.eu/en/human-regulatory/herbal-products/herbal-medicines-regulatory-scientific-support
7. Call for scientific data for use in HMPC assessment work on Cannabis sativa L., flos (Cannabis sativa flowering tops). https://www.ema.europa.eu/en/documents/herbal-call-data/call-scientific-data-use-hmpc-assessment-work-cannabis-sativa-l-flos-cannabis-sativa-flowering-tops_en.pdf
8. Medical Device Regulation 2017/745. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745
9. Medical devices EMA - https://www.ema.europa.eu/en/human-regulatory/overview/medical-devices#medicinal-products-used-in-combination-with-a-medical-device-section
10. Medical use of cannabis and cannabinoids – Questions and answers for policymaking – December 2018. https://www.emcdda.europa.eu/system/files/publications/10171/20185584_TD0618186ENN_PDF.pdf
11. Cannabis legislation in Europe – an overview: https://www.emcdda.europa.eu/system/files/publications/4135/TD0217210ENN.pdf

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