Abilify Mycite:
IP management aspects & related strategic dimensions

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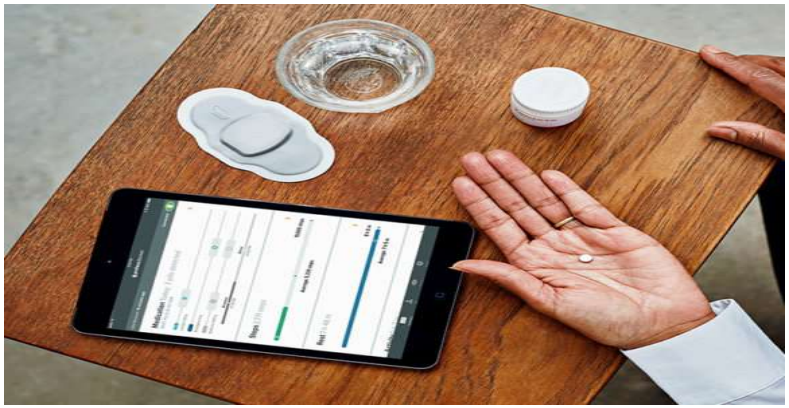
IESs and Future Combinations



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A human pilot trial of ingestible electronic capsules capable of sensing different gases in the gut

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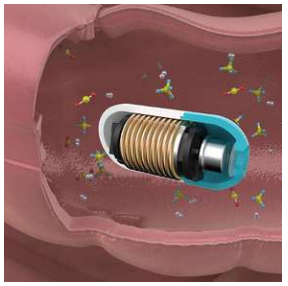

REPORT

An ingestible bacterial-electronic system to monitor gastrointestinal health

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Science 25 May 2018:

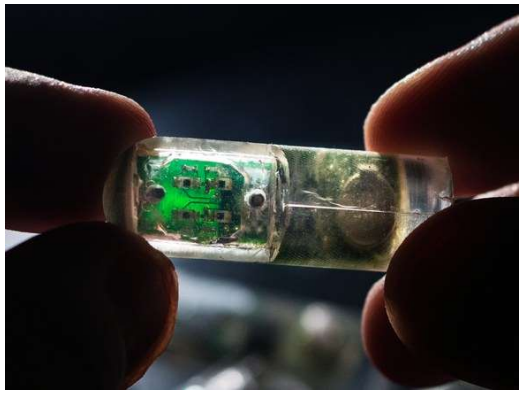


Photo Credit: LILLIE PAQUETTE/MIT

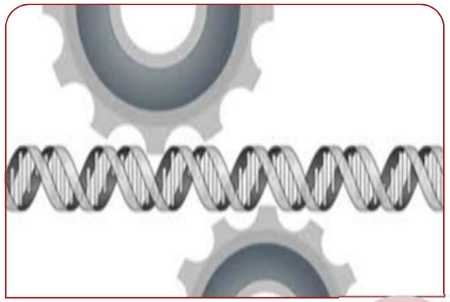
Photo Credit: ABILIFY MYCITE®

Abilify MyCite is a drug–device combination product of Proteus's ingestible electronic sensors (IES) and Otsuka's Abilify drug (aripiprazole) used to treat adults for schizophrenia, bipolar I disorder, and major depressive disorder.

The Abilify MyCite system consists of four components: Abilify MyCite (that is, aripiprazole tablets with an IES); MyCite Patch (that is, Proteus's wearable sensor); MyCite App (that is, a smartphone application); and web-based dashboards for health-care providers.

NB: Proteus filed for bankruptcy in June 2020. Court approved "stalking horse" bid from Otsuka to acquire Proteus Digital Health for $15 million.

Abilify Mycite IP aspects



PATENTS

Copyright

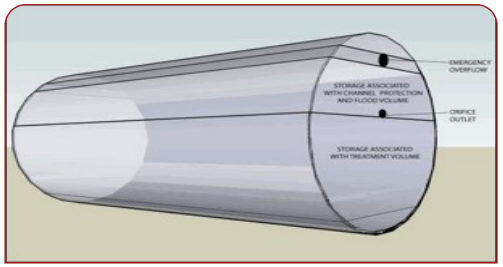
TRADEMARK

Data Base Protection

Trade Secrets

Regul. Excl.

Domain name



Design

Intro

- IP Portfolio strategy (1)
  - Start at the very beginning of the product development process (and even in pre-development R&D) to plan IP strategy
  - Make sure it is aligned with regulatory approval procedures
    - If the product protected by IP is not aligned with the product that is being authorised (for products that require regulatory approval), IP protection is not useful
  - Look at all relevant IPRs
  - Filing strategy is obviously only relevant for IP rights which require registration and are subject to examination

Intro

- IP Portfolio strategy (2)
  - Patents require most strategic preparation
    - Carry out prior art search
    - Ensure you have good insight into your freedom-to-operate position
    - What is the reason for your IP position?
    - ->Required to bring product to market
    - -> More defensive strategy, to fence off the territory for third parties and/or prevent third parties to invent around
    - Decide on the willingness to go into licensing agreements.
    - ->With complex products such as the one of this project, technology is split amongst different IP right holders (Proteus Digital Health has an IP portfolio relating to the sensor and related computer technology. Otsuka Pharmaceutical Co. Ltd has a large IP portfolio relating to the pharmaceutical compounds and formulations for aripiprazole).
    - -> (Cross-) licensing agreements are indispensable, and form an important part of the IP strategy

Timeline for obtaining IP rights in product development cycle

- For IP rights subject to registration (first filer wins), the goal must be to file as early as possible, but ensure that IP protection covers final product put to market
- Copyright is in many jurisdictions not subject to registration, but is merely invoked

Complex product

- Our product is a complex product, comprising multiple components:
  - The drug
  - The drug with sensor sending a signal
  - The patch receiving the signal and transmitting that signal to a software app
  - The software app transferring the information to a computer system (comprising inter alia patient data files)
  - Further analytical algorithms in the software of the computer system processing and interpreting the data

Multiple potential IP rights

- Copyright: for the software elements, the GUI of the software and the database
- Database right (*sui generis*) for the database
- Design: for the sensor and the patch
- Patent: for the drug, the software, the drug/sensor combination, the patch, the sensor (where applicable), a kit comprising the various components
- Trade mark protection
- Trade secret protection (in many jurisdictions, not an IP right as such, but relevant to IP)

Copyright

- Software:
  - Protects only source code, not the functionality
  - GUI can be protected under copyright as an artistic type of right
- Database:
  - Definition: "database' shall mean a collection of independent works, data or other materials arranged in a systematic or methodical way and individually accessible by electronic or other means"
  - Is protectable provided that by the selection or arrangement of the contents of the database, it constitutes the author's own intellectual creation
  - Does not protect the creation of the data

Sui generis database right

- A right for the maker of a database:
  - which shows that there has been qualitatively and/or quantitatively a substantial investment in either the obtaining, verification or presentation of the contents
  - to prevent extraction and/or re-utilization of the whole or of a substantial part, evaluated qualitatively and/or quantitatively, of the contents of that database

No property right in the data

- In most jurisdictions, there is no separate property right in the data
- There can be de facto possession, and commercial strategies can be developed based thereon

Exercise database rights or not?

- Whether one will use the database rights depends to a large extent on the business model used.
  - 1) One is to provide access to the databases by third parties for them to query
  - 2) Another business model starts from the idea that the data are not shared, but in-house algorithms are developed which can enquire the databases with a high level of sophistication. Third parties can then "indirectly" query the databases, and receive a result. Third parties will in such a scenario not obtain access to the databases themselves or to the algorithm. That will imply the use of trade secrecy as a tool for such business model.
- On trade secrets, see further below

Patent protection

- Patent protection can exist in the compound (not for Abilify, where the active ingredient is off-patent)
- Can exist in the “hybrid medicine” (drug and censor)
- Can exist in the sensor
- Can exist in the software
  - Software protects functionality
  - Must have technical effect (no problem in this case)
- Can exist in the kit (all the components together)
- Any other relevant hardware

Patent protection: examples (1)

- Otsuka Pharmaceutical Co Ltd has patent portfolio on:
  - A variety of aripiprazole formulations
  - Interestingly, a patent application, now withdrawn, for "EP3448387A1 COMPOSITIONS OF PHARMACEUTICAL PRODUCT WITH INGESTIBLE EVENT MARKER"

Patent protection: examples (2)

- Proteus Digital Health Inc has patent portfolio on:
  - EP1889198B1 PHARMA-INFORMATICS SYSTEM (which is the sensor)
  - EP2506820 (B1) INTEGRATED INGESTIBLE EVENT MARKER SYSTEM WITH PHARMACEUTICAL PRODUCT
    - 1. A pharmaceutical product comprising: a pill (20) and a device (22) including a top and a bottom, and secured to the pill, wherein the device comprises: a non-conducting skirt that defines a central cavité; a control unit positioned in the cavity defined by the skirt, wherein the control unit includes at least two dissimilar materials positioned on opposite sides of the control unit and electrically connected thereto, wherein the dissimilar material when exposed to a conducting fluid, create a voltage potential for powering the control unit and wherein the control unit, when powered, generates a current signature with information encoded in the current signature; and a securing portion (30) on the bottom of the device for securing the device to the pill.

Patent protection: examples (3)

- A patent application WO2014197402 (A1) / EP3005281 SYSTEM, APPARATUS AND METHODS FOR DATA COLLECTION AND ASSESSING OUTCOMES
  - 1. A computer-implemented method, comprising: receiving, by a computer system, ingestible event marker (I EM) system information from a receiver worn by a subject, the I EM system information comprising physiological information and information associated with ingestion of medication by the subject, wherein the receiver is configured to communicate with the computer system; receiving, by the computer system, contextual information associated with the subject; and calculating, by the computer system, a composite risk score based on a combination of the I EM system information and the contextual information associated with the subject.

Open Source Software (OSS) and effects on IP position

- Please be aware of the possible effects of the use of OSS in the product development chain
- Depending on the type of license for the use of the OSS used, it could be necessary to give a license to the additions (also patents) to anyone who is further down in the chain
- Investigate at an early stage whether you will use OSS, or whether OSS has been used in the development of the software used in the commercial products/systems

Design protection

- Under EU law, it protects the appearance of the whole or a part of a product resulting from the features of, in particular, the lines, contours, colours, shape, texture and/or materials of the product itself and/or its ornamentation
- Would be possible for:
  - The sensor
  - The patch
- However, in Europe, a Community design shall not subsist in features of appearance of a product which are solely dictated by its technical function
  - Is interpreted as meaning that the technical function is the only factor which determined those features, the existence of alternative designs not being decisive in that regard

Trade secrets

- Trade secret protection comes into play at different levels:
  - The existence of algorithms which the developer suspects will not fulfil the patentability requirements, or which he/she does not want to make public
  - De facto possession of large data sets
    - Large data sets allow the development of a separate business model, whereby the data set can be queried, without access to the data set and the algorithm, and the party querying the algorithm and the data set just received a result

- Also consider whether it is possible to obtain IP protection for some elements, whilst retaining trade secrecy for others

Trade secrets - Benefits

- Its apparent benefits are the following:
  - No obligation to disclose technical information that you do not want to see in the public
  - No formalities
  - It creates an enforceable right
  - A useful way to protect know-how that you want to some extent to remain secret
  - A useful way to protect know-how that would not be eligible for protection under other IP rights
  - Trade secrets have been proven to be rather popular, and are frequently used

Trade secrets - Drawbacks

- Its apparent drawbacks are the following:
  - There is no disclosure, hence arguably society does not benefit from addition to the stock of knowledge, to the same extent as that would have been the case if there would have been a disclosure
  - Enforcement can present specific challenges:
    - Exact scope of the secret know-how invoked can be difficult to determine
    - The secret nature is not always easy to establish or prove
    - Problem that people cannot be expected to “delete their brain” when changing job (about which more later)

Trade secrets - Drawbacks

- Can potentially provide less legal certainty, as often the perception of what is secret is rather misleading:
  - E.g., if something can be reverse engineered, it is no longer secret
  - Hybrid know-how (secret and public) makes matters often more complicated

Open Innovation

Responsible Research and Innovation

- Inclusive engagement with patients and stakeholders to co-create solutions to address product concerns in order for effective uptake
- Product adoption crucial areas such as
- AMR
- Telemedicine (COVID-19)

Accelarating digital health innovation

- Digital Medicines Society (DiMe)
- Gateone project
- Eli Lilly's open innovation challenge

Open innovation, IP and the FAIR standard

To be Findable:

F1. (meta)data are assigned a globally unique and eternally persistent identifier.
F2. data are described with rich metadata.
F3. (meta)data are registered or indexed in a searchable resource.
F4. metadata specify the data identifier.

To be Accessible:

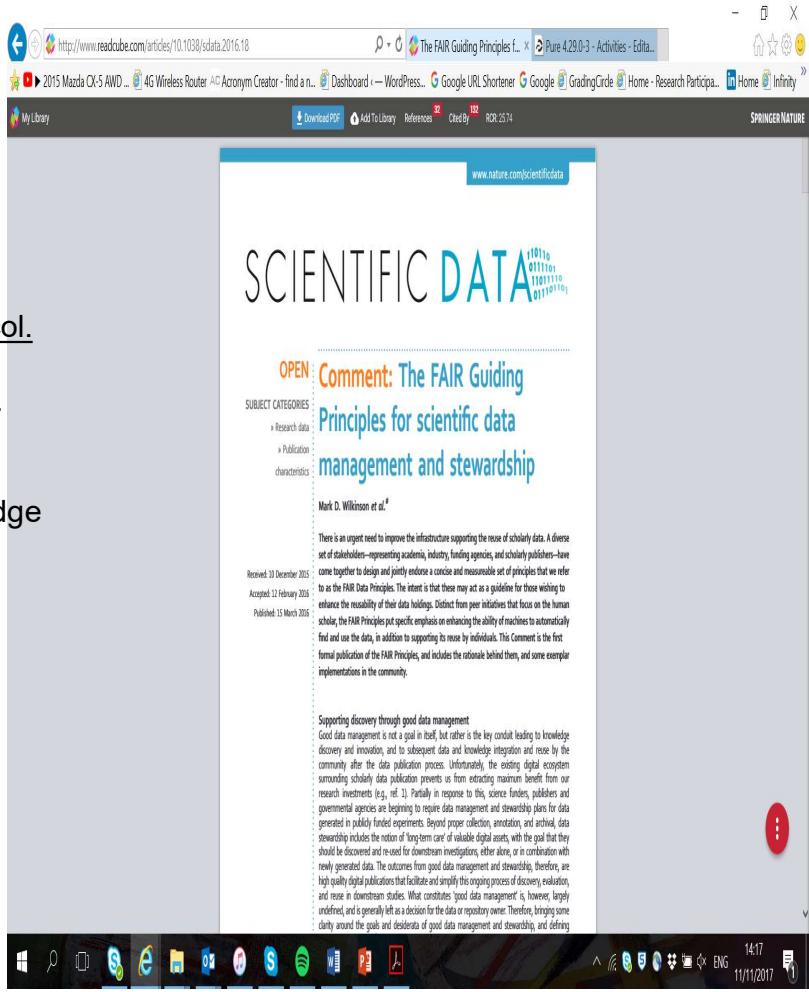
A1 (meta)data are retrievable by their identifier using a standardized communications protocol.
A1.1 the protocol is open, free, and universally implementable.
A1.2 the protocol allows for an authentication and authorization procedure, where necessary.
A2 metadata are accessible, even when the data are no longer available.

To be Interoperable:

I1. (meta)data use a formal, accessible, shared, and broadly applicable language for knowledge representation.
I2. (meta)data use vocabularies that follow FAIR principles.
I3. (meta)data include qualified references to other (meta)data.

To be Re-usable:

R1. meta(data) have a plurality of accurate and relevant attributes.
R1.1. (meta)data are released with a clear and accessible data usage license.
R1.2. (meta)data are associated with their provenance.
R1.3. (meta)data meet domain-relevant community standards.



Regulatory Aspects

Abilify Mycite: combination product where prescription drug product is embedded with an IES

- Combination product in the US; approved by FDA
- Medicinal product in the EU; no current marketing authorization in the EU

Medical Devices Regulation

- IES regulated as a Class II medical device

Digital evergreening

- aripiprazole is generically available but when used in combination with IES, market exclusivity could be gained

Clinical Trials Data transparency, Trade Secrets & The CJEU

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Protection of technical solutions concerning PRIVACY, & ETHICS & CYBERSECURITY: An increasingly important factor?

Conclusions

- IESs are a **promising technology** for improving health outcomes and making health care more effective
- The often overlapping **IP, Privacy, and Ethical issues should be considered at the earliest stages** of the development process of such products.
- Consider links between IP and sustainability/responsibility/regulatory compliance
- Consider links between IP and privacy, ethics & cybersecurity (by design) technologies:
- For IESs products to be trusted and broadly accepted by society and markets, these „links“ are becoming an increasingly important factor for competitiveness and compliance.

Further reading (no-IP focus):

Gerke, S., Minssen, T., Yu, H. *et al.* Ethical and legal issues of ingestible electronic sensors. *Nature Electronics* **2,** 329–334 (2019). https://doi.org/10.1038/s41928-019-0290-6

Thanks! Questions or Suggestions?

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