EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Experience and opportunities for the Co-development (process) of Companion Diagnostics and Medicinal Products (in the EU)

EMA stakeholder platform meeting - 25th April 2017

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Outline

- Background
- Biomarker Qualification
- Experience and opportunities with the co-development of medicinal products (MPs) and companion diagnostics (CDx)
- Advances in the co-development process for personalised medicines

Background:

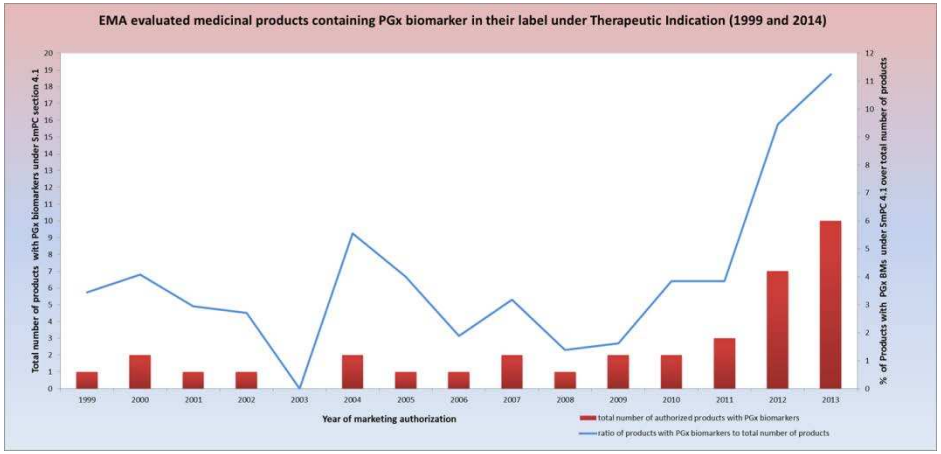
Companion Diagnostics: The Expanding Reach Of Personalized Medicine

14 Mar 2017 **ANALYSIS**

Executive Summary

Personalized medicine is becoming the hallmark of care in oncology, but its use is also increasing in other therapeutic areas including inflammation, respiratory, infectious diseases and central nervous system disorders, as scientific understanding of these diseases advances. The expansion of companion diagnostics beyond oncology has impacts on dealmaking, clinical practice and the R&D pipeline.

SCRIP



An analyses of the patient population studied (BM+ and/or –) in the pivotal trial submitted for initial MAA leading to marketing authorisation and biomarker inclusion in the therapeutic indication section of the product label showed that…..**only 10 out of 30 products (1/ 3) have been including biomarker positive and negative patients in their pivotal clinical trial**.

The Pharmacogenomics Journal (2015), 1 – 10

EMA Qualification of novel methodologies for medicine development

CHMP Qualification Advice on future protocols and methods for further method development towards qualification

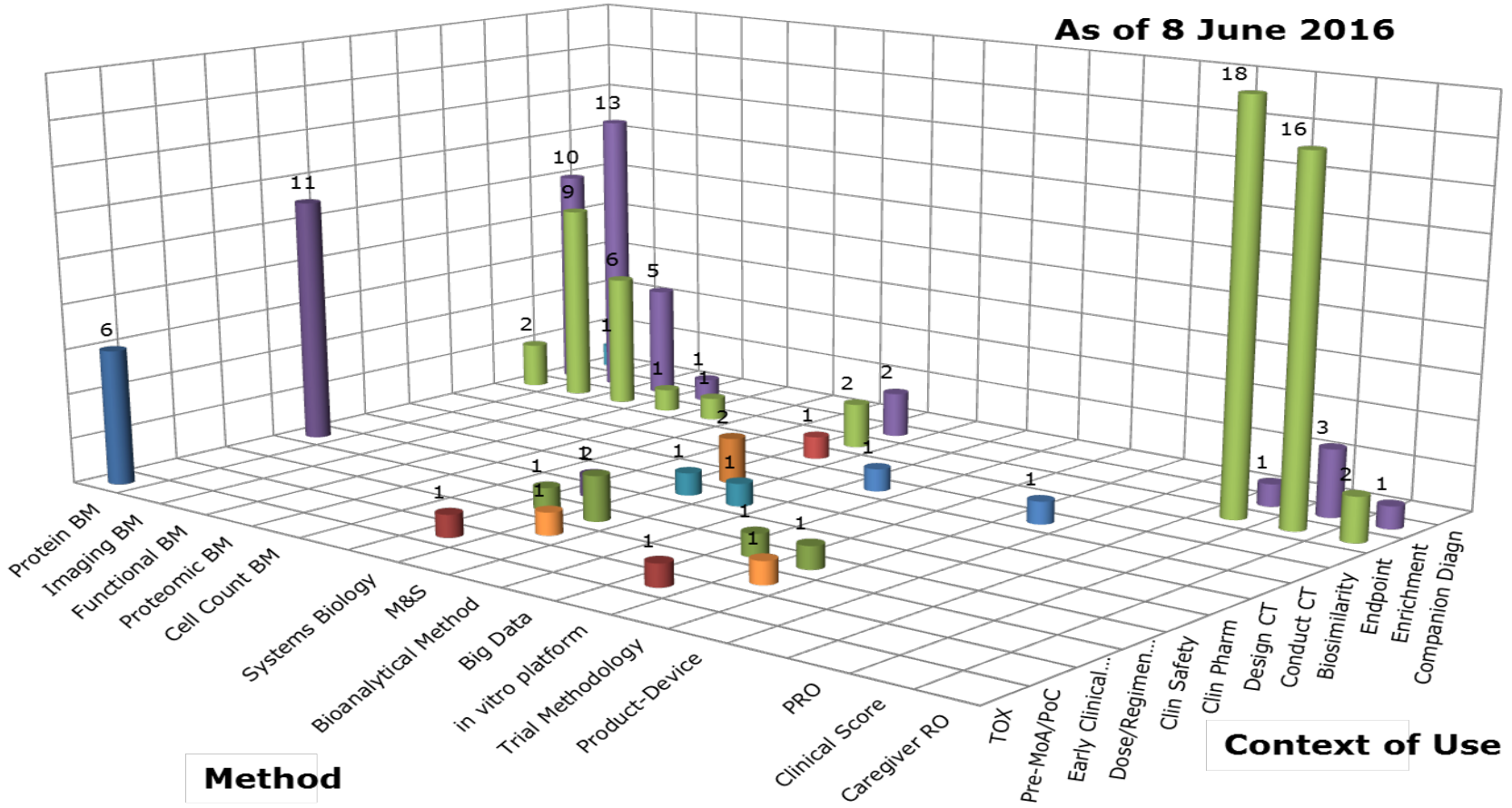
CHMP Qualification Opinion on the acceptability of a specific use of the proposed method (e.g. use of a biomarker) in a research and development (R&D) context (non-clinical or clinical studies), based on the assessment of submitted data

Fees & Exemptions applicable

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/06/WC500208145.pdf

Who can apply? Consortia, Networks, Public/Private partnerships, Learned societies, Pharma, CROs, Software developers,...

Vision: Speed up/optimise drug development and utilisation, improve public health


As of 8 June 2016
Protein BM
Imaging BM
Functional BM
Proteomic BM
Cell Count BM
Systems Biology
M&S
Bioanalytical Method
Big Data
in vitro platform
Trial Methodology
Product-Device
PRO
Clinical Score
Caregiver RO
TOX
Pre-MoA/PoC
Early Clinical...
Dose/Regimen...
Clin Safety
Clin Pharm
Design CT
Conduct CT
Biosimilarity
Endpoint
Enrichment
Companion Diagn
Method
Context of Use

Experience and opportunities for the co-development of Medicinal Products and Companion Diagnostics (CDx)

- Recruitment of **diagnostic/ BM negative patients** in pivotal trial
- **Concordance testing**
  - between development stages (clinical trial assay (CTA) and the market ready assay (MRA))
  - across indications
  - between different assays
- **Analytical CDx validation** (cut-off values, sensitivity and specificity, reproducibility, cross validation)

Experience and opportunities for the co-development of Medicinal Products and Companion Diagnostics (CDx)

- Clinical utility

- Information of CDx in the medicinal product labelling
  - Mandatory vs. optional testing (companion vs. complementary diagnostic)

- Prospective versus retrospective validation / use of historical data

- Impact of different approval pathways on co-development process (adaptive licensing, PRIME, conditional approval)

Concept paper on the co-development of biomarker-based companion diagnostics and medicinal products in the context of drug development DRAFT

1/ Recommendations for the **co-development** of medicinal products and biomarker-based assays

2/ **CDx development during the marketing phase** of the medicinal product

3/ **Labelling**, European public assessment reports (EPARs) and the risk management plans (RMPs)

4/ Regulatory **procedural aspects** for the co-development of medicinal product and CDx

Anticipated time table for the development of guidance on medicinal product – CDx co-development:

- June/July 2017: Publication of DRAFT Concept paper for 3-5 months public consultation

EMA's future role for companion diagnostic development

Press release - Public health – 05-04-2017 - 12:47

Adoption of a Regulation on **in vitro diagnostic medical devices**

IVDR Article 2(7)

Companion diagnostic means a device which is **essential for the safe and effective use of a corresponding medicinal product** to:

- **identify**, before and/or during treatment, **patients** who are most likely to **benefit** from the corresponding medicinal product; or
- **identify**, before and/or during treatment, **patients** likely to be at **increased risk for serious adverse reactions** as a result of treatment with the corresponding medicinal product

EMA's future role for companion diagnostic development

IVDR Article 48(3)

For **companion diagnostics** the **notified body** shall **consult** the concerned **competent authority** designated in accordance with Directive 2001/83/EC or the European Medicines Agency (**EMA**), as applicable

ANNEX IX, Chapter II - 5.2. Assessment of the technical documentation of companion diagnostics

The notified body shall, before issuing an EU technical documentation assessment certificate for the companion diagnostic and **on the basis of the draft summary of safety and performance** [..] consult one of the competent authorities [..] **regarding the suitability of the device in relation to the medicinal product concerned**.

EMA's current role in review of medicinal product and medical device combinations

Hemostatic matrices

Drug delivery medical devices in medicinal products

- Non-integral (CE-mark required prior to CHMP opinion)
- Integral (No CE mark required)

Medicinal substances incorporated in medical devices (Ancillary)

- Consultation of NB with NCA/EMA
- Established procedure and guidance for initial and post-consultation

ATMP combination products

- One or more medical devices as an integral part of the medicine
- Existing procedural advice on the consultation of Notified Bodies

Challenges in (co-)development of companion diagnostic and medicinal product

- No requirement of simultaneous development of CDx and medicine from beginning to end
- Co-development should generally facilitate contemporaneous marketing authorizations for the medicinal product and the associated IVD companion diagnostic - but not a requirement
- New IVDR specifies timeframe (max 120 days) for scientific opinion

New yet-to-be defined process – 60 (120) Day timetable*

NB review of technical file of CDx

Request from NB to EMA
Draft summary of safety and performance
Draft instructions for use

D0 Validation

D36 Assessment by CHMP Rapporteur

D50 CHMP comments

Clock Stop

Request for supplementary information

CHMP opinion

Public Assessment Report

D60 or D120

No EC decision

Notified body

NB convey final decision to EMA

CE mark for CDx

* Example in analogy to type II variations

Outlook

- ✓ Impact Assessment of new MDR and IVDR on EMA and network
  - ➢ e.g. new consultation procedures, clinical trial regulation
- ✓ Drafting of implementation plan
  - ➢ Involvement of different and new stakeholders within and outside network
  - ➢ Establishing (new) relationships, cooperation and exchange of information

Thank you for your attention

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