Towards a 21st Century Regulator’s role
EMA Early Access Toolbox

Bulgarian Presidency Conference on “Health as the Real Winner: Presidency Conference on Options to Provide Better Medicines for All”

6 March 2018, Sofia

Zaide Frias
Head of Human Medicines Evaluation Division, EMA
21st Century Regulator’s Role is about connecting the dots and building right links.

- Facilitate development and access to medicines
- Evaluates applications for Marketing authorisation
- Provides information to healthcare professionals and patients
- Protects human and animal health
- Building a common Vision
Facilitating research and development – EMA Early access toolbox

Medicines & Technology Horizon scanning

Research & Development support

EU Regulatory pathways

Cost of Development

Innovation Task Force Business Pipeline

SA /Parallel HTA Orphan /Paediatric ATMP/SME

PRIME/Adaptive pathways/Best evidence generation

Incentives/Innovative Medicines Initiative (PPP)/ Horizon 2020/

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EU Regulatory Pathways

PRIME – PRI ORITY ME DICINE S

>160 eligibility requests
34 granted

Single Source

Adaptive Pathways

Multiple Sources

### Time difference vs. EC approval date (months)

<table>
<thead>
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<th>INN (trade name)</th>
<th>Indication</th>
<th>NICE</th>
<th>SMC</th>
<th>GBA</th>
<th>HAS</th>
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*first in class

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Experience with parallel regulatory/HTA discussion on evidence generation plans

Number of parallel advice

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<td>2016</td>
<td>24</td>
</tr>
<tr>
<td>2017</td>
<td>24</td>
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</table>

Level of alignment

- Full agreement
- Partial agreement
- Disagreement

Level of agreement (HTABs vs. regulators; N = 31 procedures):
- Population
- Comparator
- Endpoints
- Other study design characteristics
- Overall efficacy and safety data package

British J Clin Pharm, Volume 82, Issue 4, pages 965-973

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5 October 2017
The Digital Revolution in Medicine is taking place now.

From Chatbots to Artificial Intelligence

From Big data to the Health Cloud

New role for regulators
Science and technology is advancing at exponential pace

**Omnics**
- Personalised medicines/Biomarkers

**Data**
- DNA
- Protein
- Antibody
- Metabolite
- Biome

**Life Style**
- Exercise
- Environment
- Behavior
- Treatment
- Diet

**Modelling & Simulation**
- Extrapolation

**Digital health and wearable technology**
- Gene therapy/cells and tissues based products
‘...Technologies which could change our lives: potential impacts & policy implications...’ (Source EP STOA’s)

**Wearable technologies:**
‘From physical electronic devices to new types of ‘smart fabrics’, the reasons for wearing our clothes are changing. How will this change our data-sharing habits and the way healthcare is delivered?’

- Health Apps and their evaluation and regulation
- CT data capturing software / home reporting programs

**Smart home technologies:**
‘The Internet of Things now increasingly includes electronic devices operating in our homes. How will our everyday behaviours and personal relationships change as a result?’ (ENISA)

- Integrated Health and Health Care reporting / monitoring early warning signals to prevent longer / severe hospitalisation


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New competences are required for regulatory and public health systems, both for evaluation and delivery to patients.
Borderline products (MP-MD) / Novel technologies

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From Regulatory Optimisation to Digital transformation

Novel enabling technology development

Utilisation for Regulatory Processes
Need to widen the collaborations’ horizon

McLaren partnership
GSK and the McLaren Group are working together to help drive innovation and performance across our business.

Have feedback? We’d like to hear from you. Write me at: 

GOOGLE'S LATEST DIGITAL HEALTH MOVES: At the North America (RSNA) conference, Google announced strategic IT partnerships in the healthcare space. The partnerships each computing platform, Google Cloud, to give medical providers workflows, lower costs, and improve efficiency.
Path Towards a 21st Century Regulator’s role

Pursues regulatory optimisation

Embraces digital transformation

Develops new competences

Interacts with new players
Further information
Zaide Frias, Head of Human Medicines Evaluation Division

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Back up slides:

PRIME builds on existing Regulatory tools
Scientific advice

- Sponsors prefer early interactions
- Earlier SA is associated with higher MAA success rate
- Compliance with SA recommendations on clinical trial design associated with
  - Higher MAA success rate
  - Less major objections
  - Shorter MAA procedure

Nature Reviews Drug Discovery

Reasons for reverting to standard timelines during the MAA evaluation, include:

- Major clinical objection questioning the clinical relevance of the effects
- Numerous major objections including need for re-analysis of efficacy data
- Major objection on adequacy of extrapolation
- Significant quality major objection
- Critical GCP issues identified in inspections
- Need for a GMP inspection

Robust decision making under accelerated timelines requires a mature submission, which should be subject to pre-filing discussions.

In 2017, 58% of Accelerated assessment timelines were maintained till Opinion

Accelerated assessment requests

<table>
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<th>Year</th>
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Conditional Marketing Authorisation

Overview of Conditional marketing authorisations by year of granting and current status

Importance of early dialogue and prospective planning

CMAs by stage of procedure when CMA was first considered

Average duration of procedure (including clock-stops) by stage of procedure when CMA was first considered
Regulatory and HTA Interactions

Current paradigm

- Regulators
  - Quality, safety, efficacy (first 3 hurdles)
  - Benefit–risk profile
  - Emphasis on RCT, most often placebo-controlled

- Payers
  - Relative efficacy/effectiveness
  - Cost versus health benefit,
  - Budget impact (4th hurdle)

Future paradigm?

- Regulators
  - Quality, safety, efficacy
  - Benefit–risk profile
  - Relative efficacy/effectiveness

- Payers
  - Cost versus health benefit,
  - Budget impact
  - Relative efficacy/effectiveness

- Emphasis on RCT, most often active- and placebo-controlled

- Assessors
  - Active-controlled RCT
  - Observational studies
  - Cost-effectiveness/ utility analyses
  - Budget impact analysis

- Assessment Focus
  - Cost-effectiveness

- Studies/data
  - Active-controlled RCT
  - Adaptive Phase III–IV trials
  - Observational studies
  - Meta-analysis