Experience with the ITF framework for 3Rs and new approach methodologies (NAMs)

Industry stakeholder platform on research and development support

11 July 2022
EMA and the 3Rs

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- EMA actions on 3Rs in 2016-17
- Scientific guidelines
- Veterinary medicine testing outside the EU
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This context applies to human and veterinary medicines

The European Medicines Agency (EMA) supports the implementation of the so-called 3Rs principles - replace, reduce and refine - for the ethical use of animals in medicine testing across the European Union (EU). These principles encourage alternatives to the use of animals in the testing of medicines while safeguarding scientific quality and improving animal welfare where the use of animals cannot be avoided.

Directive 2010/63/EU requires marketing authorization holders to integrate the 3Rs and welfare standards for the treatment of animals in all aspects of the development, manufacture and testing of medicines.

The Directive aims to protect animals in scientific research, with the final aim of replacing all animal research with non-animal methods.


NEW
Start of CHMP/CVMP Joint 3Rs Working Party – Q3/4 2022
Driving the Regulatory Science and EU Network Strategy together with all stakeholders
Refocus the role of the Joint 3Rs WG to **support qualification** of new alternative 3Rs methods.

Innovation Task Force (ITF)

Multidisciplinary platform for preparatory dialogue and orientation on innovative methods, technologies and medicines

Support innovative drug development

Early informal dialogue with opinion leaders on
- Scientific, legal and regulatory issues
- Products, methodologies and technologies

Free of charge

Brainstorming “style” on innovation in areas without existing guidance

First step to engage is submit completed 3-page template

Contact:
itfsecretariat@ema.europa.eu for human medicines
itfvet@ema.europa.eu for veterinary medicines
Number of ITF BMs in 2021 (and before)

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of meetings</th>
<th>Number of EMA participants</th>
<th>Number of NCA participants</th>
<th>Number of Stakeholder participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>26</td>
<td>166</td>
<td>115</td>
<td>148</td>
</tr>
<tr>
<td>2018</td>
<td>23</td>
<td>129</td>
<td>106</td>
<td>126</td>
</tr>
<tr>
<td>2019</td>
<td>26</td>
<td>167</td>
<td>118</td>
<td>165</td>
</tr>
<tr>
<td>2020</td>
<td>30</td>
<td>189</td>
<td>248</td>
<td>286</td>
</tr>
<tr>
<td>2021</td>
<td>38</td>
<td>251</td>
<td>347</td>
<td>347</td>
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</table>
ITF is now also focusing on the regulatory acceptance of so-called new approach methodologies (NAMs) to replace the use of animals in the testing of medicines, in line with the 3Rs principles

→ e.g., \textit{in silico} modelling & novel \textit{in vitro} assays (e.g. MPS/OoCs, Organoids)

**Objectives:**

- To increase the number of ITF meetings focused on NAMs
- To increase awareness and fill in the gap between EMA and developers
- To accelerate the integration of NAMs in the regulatory framework for the development and evaluation of medicines
### Number of ITF BM requests related to 3Rs (2020 – 2022)

<table>
<thead>
<tr>
<th>Relation to 3Rs</th>
<th>Type of development</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. New approach methodology</td>
<td>Organ-on-a-chip / organoid</td>
</tr>
<tr>
<td>2. New approach methodology</td>
<td>Organ-on-a-chip</td>
</tr>
<tr>
<td>3. New approach methodology</td>
<td>Organ-on-a-chip / 2D and 3D culture models</td>
</tr>
<tr>
<td>4. New approach methodology</td>
<td>Animal-free antibody production/testing</td>
</tr>
<tr>
<td>5. New approach methodology</td>
<td>Alternative transgenic animal model for the evaluation of EDs</td>
</tr>
<tr>
<td>6. 3R-related questions:</td>
<td>Antisense oligonucleotide therapy for very rare mutations</td>
</tr>
<tr>
<td>Validity of <em>in vitro</em> methods for toxicity studies?</td>
<td></td>
</tr>
<tr>
<td>Are animal studies mandatory?</td>
<td></td>
</tr>
<tr>
<td>7. 3R-related question:</td>
<td>Consortium for CAR-T Cell Therapies</td>
</tr>
<tr>
<td>Validity of <em>in vitro</em> and <em>ex vivo</em> methods for toxicity studies</td>
<td></td>
</tr>
<tr>
<td>Which read out is considered relevant for such assay?</td>
<td></td>
</tr>
<tr>
<td>8. 3R-related question:</td>
<td>Peptidomimetics technology</td>
</tr>
<tr>
<td>Validity of <em>in vitro</em> methods for efficacy studies</td>
<td></td>
</tr>
</tbody>
</table>
What do we want to discuss in the 3Rs ITF meetings?

- Test methodology (protocol, endpoints)
- Context of use (including limitations).
- Relevance within a particular context of use
- Gold standards used per endpoint
- Applicability of biomarkers

- Need of a specific guidance for method developers on qualification
- Develop endpoint-specific performance standards incl. list of reference compounds (positive & negative controls)
- Follow-up procedures to support regulatory acceptance (e.g. SA, QA, safe harbour)

Guideline on the principles of regulatory acceptance of 3Rs testing approaches

First EMA workshop on non-animal approaches in support of medicinal product development
Q & A session

- What are the main areas of interest to industry with regards to the regulatory acceptance of 3Rs?

- Is industry interested in presenting methods through ITF, either alone or as consortium? What are the perceived hurdles?

- Is there an interest to further interact to foster regulatory acceptance of Microphysiological systems (MPS)/Organ-on-chips (OoC)?
Special thank to:
Blanquie Oriane (ITF Office) and Falk Ehmann (ITF Office)

Any questions?

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