Overview

PAREXEL Informatics is a leading imaging core lab with the experience and ability to provide a wide range of services in clinical trials. PAREXEL Informatics Medical Imaging consists of 400+ global staff, we process ~13,000 images monthly from 85k+ sites, have managed 1425+ trials, over 74 regulatory approvals and 2.5+ million imaging timepoints.

The Central Nervous System (CNS) and Ophthalmology groups within PAREXEL Informatics understand the unique and custom requirements of Neuro-Ophthalmology trials and have the flexibility, creativity, bandwidth, and understanding already in place to effectively manage and support these clinical trials.

Neuro-Ophthalmology Considerations\(^1,2\)

- Ophthalmic imaging procedures (Optical Coherence Tomography (OCT), Fundus Autofluorescence (FAF), Color Fundus Photography (CFP) etc.) are rapid non-invasive imaging tools to evaluate retinal toxicity due to administration of pharmacologic compounds in CNS diseases.
- Retinal Nerve Fiber Layer Thickness (RNFLT) and macular volumes generated using OCT imaging have been shown to correlate with clinical measures of vision loss (e.g. low-contrast letter acuity and visual field analyses).
- Retinal imaging technologies (OCT and potentially others) may allow for the visualization of disease process in Multiple Sclerosis (MS) and may be useful in longitudinal monitoring of neuroprotection in response to therapeutic agents.
- The retina offers an excellent opportunity to non-invasively image neuronal tissue, and develop ocular biomarkers for various CNS disorders, e.g., Alzheimer’s disease, MS, etc.
- Due to the quick changes in Retinal Nerve Fiber Layer thickness (RNFLT) after acute optic neuritis (ON), neuro-protective strategies can be tested in ON patients over a short time frame with precise and reproducible measures that can be generated using OCT imaging.

\(^1\) Frohman et al., Nature Clinical Practice, Neurology, 2008, 4(12)
\(^2\) Costello et al., Ophthalmic Surgery, Lasers & Imaging, 2011, 42(4)

PAREXEL Informatics Advantages:

- Central review of brain and ophthalmic imaging occurs through one source providing efficiencies and risk reduction
• Access to experienced and dedicated interdisciplinary teams including Key Opinion Leaders
• A team with significant experience mitigation logistical challenges of connecting a neurology site with an ophthalmology center.
• Deep technological expertise to support multiple OCT scanner vendors for analysis.

Experience

PAREXEL Informatics Medical Imaging partners with the appropriate reading center to provide the scientific expertise to consult on any study, which includes MDs and PhDs who specialize in the following indications:

• Optic Neuritis, Optic neuropathy
• Stroke
• Multiple Sclerosis
• Alzheimer’s Disease

PAREXEL Informatics Medical Imaging is also equipped with internal full-time ophthalmic imaging experts including PhDs, Certified Retinal Angiographers (CRA) and OCT-Certified (OCT-C) professionals with more than five years of experience in OCT, Fluorescein Angiography, ICG Angiography, Color Fundus Photography, Visual Fields, Microperimetry, and additional photography (FAF, Infrared, Red Free).

PAREXEL Informatics Medical Imaging has been supporting 98 neuro-imaging clinical trials.
PAREXEL Informatics Medical Imaging is supporting ten ongoing ophthalmic clinical trials.

<table>
<thead>
<tr>
<th>Study #</th>
<th>Phase</th>
<th>Start Date</th>
<th>End date</th>
<th>Indication</th>
<th>Modalities*</th>
<th># of Sites</th>
<th># of Patients</th>
<th>Review Criteria**</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>7/12/2012</td>
<td>7/1/2016</td>
<td>Alzheimer’s Disease</td>
<td>OCT, CFP, FAF, &amp; Iris photography</td>
<td>225</td>
<td>2000</td>
<td>Safety, change over time: RPE and ONL Thickness, Hypo-and Hyper- fluorescence, Drusen Area (AREDS)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Other abnormalities:</strong> RPE Volume, RNFL Thickness, Subretinal exudation, Vitreoretinal Interface, Iris Pigmentation, Area of GA, Hypo- and Hyper- pigmentation</td>
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<td>2</td>
<td>2b/3</td>
<td>8/14/2013</td>
<td>3/1/2018</td>
<td>Alzheimer’s Disease</td>
<td>OCT, CFP, FAF, &amp; Iris photography</td>
<td>235</td>
<td>1500</td>
<td>Same as Study #1</td>
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<tr>
<td>3***</td>
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<td>9/1/2013</td>
<td>1/15/2016</td>
<td>Diabetic Macular Edema</td>
<td>OCT, FA, CFP</td>
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<td>200</td>
<td>CRT, Fluorescein Leakage, and Diabetic Retinopathy (ETDRS severity scale)</td>
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<tr>
<td>4</td>
<td>1</td>
<td>3/31/2014</td>
<td>6/1/2014</td>
<td>Hepatitis C</td>
<td>OCT</td>
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<td>50</td>
<td>Retina thickness, Foveal Thickness, Pathology</td>
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<td>5***</td>
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<td>10/01/2014</td>
<td>12/1/2015</td>
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<td>OCT, FA, CFP</td>
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<td>CRT, Lesion Thickness, Subretinal Fluid Thickness, CNV Size, PED Thickness, Fibrosis</td>
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<td>6***</td>
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<td>11/15/2014</td>
<td>2/15/2016</td>
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<td>OCT, FA, CFP</td>
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<td>CRT, Lesion Thickness, Subretinal Fluid Thickness, CNV Size, PED Thickness, Fibrosis</td>
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<td>7***</td>
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<td>1/2/2015</td>
<td>2/15/2016</td>
<td>Wet AMD</td>
<td>OCT, FA, CFP</td>
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<td>46</td>
<td>CRT, Lesion Thickness, Subretinal Fluid Thickness, CNV Size, PED Thickness, Fibrosis</td>
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<td>8***</td>
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<td>1/30/2015</td>
<td>4/30/2020</td>
<td>Geographic Atrophy</td>
<td>OCT, FA, FAF, CFP, NIR, MP</td>
<td>100</td>
<td>360</td>
<td>Macular Functional Response (via MP), and change in Geographic Atrophy Lesion size over time</td>
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<tr>
<td>9***</td>
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<td>1/30/2015</td>
<td>4/30/2021</td>
<td>Geographic Atrophy</td>
<td>OCT, FA, FAF, NIR, CFP</td>
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<td>200</td>
<td>Geographic Atrophy Lesion size over time</td>
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<tr>
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<td>9/15/2016</td>
<td>Wet AMD</td>
<td>OCT, FA, CFP</td>
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<td>96</td>
<td>CRT, Lesion Thickness, Subretinal Fluid Thickness, CNV Size, PED Thickness, Fibrosis</td>
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<tr>
<td>11***</td>
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<td>6/30/2015</td>
<td>3/30/2018</td>
<td>Geographic Atrophy</td>
<td>OCT, FA, FAF, NIR, MP</td>
<td>20</td>
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<td>Macular Functional Response (via MP), and change in Geographic Atrophy Lesion size over time</td>
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<td>9/01/2017</td>
<td>DME</td>
<td>OCT, FA, CFP</td>
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<td>Central Retinal Thickness, Macular Perfusion and Vascular leakage</td>
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<td>13</td>
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<td>05/01/2016</td>
<td>02/1/2018</td>
<td>Anemia</td>
<td>CFP</td>
<td>50</td>
<td>300</td>
<td>Retinal Bleeding and Diabetic Retinopathy Severity</td>
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</tbody>
</table>

*Optical Coherence Tomography (OCT), Color Fundus Photography (CFP); Fluorescein Angiography (FA); Fundus Autofluorescence (FAF), Near-infrared (NIR), Microperimetry (MP)

** Central Retinal Thickness (CRT), Retinal pigment epithelium (RPE), Retinal Nerve Fiber Layer (RNFL); Outer Nuclear Layer (ONL), Pigment Epithelial Detachment (PED), Choroidal Neovascularization (CNV); Vitreomacular Traction (VMT), Epiretinal Membrane (ERM), Geographic Atrophy (GA), Age-Related Eye Disease Study (AREDS), Early Treatment Diabetic Retinopathy Study (ETDRS)

*** Studies that include imaging based eligibility reporting
Summary

PAREXEL Informatics operational bench strength, site and image processing capability via a global footprint in combination with the expertise offered by an experienced reading center makes for an ideal study management structure. Leveraging expertise across each lab, including PAREXEL systems and export capability, will reduce the added workarounds by the Sponsor. Detailed research into Ophthalmic imaging modalities and partnership with a Key Opinion Leader (KOL) and several well recognized Reading Centers allows us to offers a robust service that, to date is not offered by any other imaging CRO (iCRO).

There are numerous advantages by partnering with a large global CRO Imaging Laboratory like PAREXEL Medical Imaging, and an industry leading reading center. The advantages are:

- A global presence and around-the-clock site support, with PAREXEL offices located in:
  - Massachusetts, USA
  - Berlin, Germany
  - Hyderabad, India
  - Kobe, Japan
- Experience supporting over 74 regulatory approvals and 93 regulatory submissions
- In-house Quality department ready to support potential regulatory agency audits.
- Several active protocols supporting ophthalmic imaging endpoints.
- Access to more than 100 Ophthalmologists, ocular disease experts and to more than 60 neuroradiologists and neurologists
- Expert readers that utilize FDA-approved PAREXEL technology that is 21 CFR Part 11 compliant