Supplementary Material

Appendix 1: Data entry forms

The database structure is depicted in Figure S1A. Patients are entered into the RD5000db database by the basic patient data form (Figure S1B). Personal data including date of birth, initials and gender are registered at patient enrollment in RD5000db for the use of a check on double entries of a single patient. After registration of the patient, only the year of birth remains visible, whereas initials are not visible to users after the basic patient data form has been saved. Other details that are entered in this form are the centers the patient visited, including the patient’s internal registration number and responsible physician, with a maximum of three centers.

The patient history form (Figure S1C) contains modules on the initial diagnosis, visual and general symptoms, ophthalmic history, medication and family history. Seven visual complaints most prevalent in IRDs and 16 syndromic features present in syndromic IRDs are documented, with the possibility to specify each complaint further with e.g. age at onset of this specific complaint or its location (if applicable). The module on family history registers data on the patient’s siblings, as well as the generations of the patient’s parents and children.

The genetics/DNA sample form (Figure S1D) primarily states the presence of a DNA sample of this specific patient. Additionally, both causative and non-causative variants can be registered. If the effects of a mutation are not known, these variants are registered in the ‘mutations of uncertain pathogenicity’ module. The correct module appears based on the conclusion of genetic analysis that was selected. The method used for genetic analysis can be specified further as well as version numbers of used gene sets, kits etc can be registered. Gene names are registered in HGNC nomenclature, whereas both complementary DNA changes and protein changes are noted for the variants/mutations.

In the clinical examination form (Figure S1E), data of ophthalmic examinations are registered, including visual acuity (including subjective refractive error), fixation, eye motility, intra-ocular pressure and slit-lamp biomicroscopy of the anterior segment and posterior segments. Except for fixation and eye motility data, all data are entered for each eye separately. Each module contains a
button to copy data of the right eye to the fields of the left eye, since IRDs are generally symmetrical.

Data of the anterior and posterior segments are entered by a drop-down menu stating the options ‘normal’, ‘abnormal’ and ‘not applicable’. Additional fields to specify observations appear if the option ‘abnormal’ is selected. If the data entry fields do not cover the observed details, a free text field enables registration of these additional data.

The technical examination form (Figure S1F) enables registration of data acquired from perimetry, color vision tests, full-field or multifocal electoretinography (ERG), electro-oculography (EOG), dark adaptation, and commonly used imaging techniques, including fundus photography, optical coherence tomography (OCT), fundus autofluorescence (FAF) and fluorescein angiography (FA). Like the clinical examination form, all data are entered for each eye separately and buttons to copy data from the right to the left eye fields are present. Furthermore, each module contains the option to upload a file, e.g. a scan of the perimetric results, the ERG graphs or digital files of imaging examinations.

The diagnoses form (Figure S1G) enables registration of the diagnoses made in the patient. The final ophthalmic diagnosis is selected from an extended list of retinal diagnoses and syndromes. Other ophthalmic diagnoses or general relevant diagnoses can be entered from the 10th revision of the International Classification of Diseases (ICD-10).

Four different field types are used in the database: value lists, check boxes, radio buttons and iterate values/dates. The default value for most value lists is “Please select…”. All value lists contain a “not applicable” value, which means these data are not available, in contrast to “not known”, which should be used if the patient cannot provide the data. Radio buttons are only used in the technical examination form, mainly to specify if the examination referred to has been performed.

To enhance usability, we minimized the amount of mandatory fields. Mandatory fields include the examination date in both clinical and technical examination forms, because the saved forms are arranged by these dates. The technical examination form has multiple mandatory fields, which specify whether an examination has been performed or not.

Appendix 2: Costs
The basic technical set-up costs of the database, with Ophthabase as a basic structure, were approximately €85,000. Based on the current use that includes 11 centers, the running costs are about €1,000 per month, which warrants maintenance, system stability, regular back-up of the database and of the source code, security updates and support. On top of that, the consortium manager spends 6 hours per week on both organizational tasks of the consortium and system administration. Currently, the costs can be covered by the funding from Dutch blindness foundations.