NIDDK IBD Genetics Consortium
Phenotype Operating Manual

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RECRUITMENT METHODOLOGY

The original goal of this consortium was to recruit 350 IBD-affected index subjects in the general form of 250 case/controls and 100 trios (affected index subject/proband plus both parents; either, neither, or both parents, can be affected) from each of the six Genetics Research Centers (GRCs). Johns Hopkins and Cedars-Sinai are recruiting minority populations, and their recruitment goals are somewhat less.

The modified goal (April 2006), based on our repository demographics thus far, is to recruit additional Ashkenazi Jewish subjects (UC or CD); additional UC subjects but exclude any UC cases with proctitis only (if possible); Toronto should keep collecting pediatric trios (UC or CD). These recommendations do not apply to Johns Hopkins or Cedars-Sinai, though they centers should modify their recruitment to include Ashkenazi Jewish and UC subjects.

An index subject should be recruited only if he/she believes a single matched control or both parents (see page 15) would be willing to participate. It is inevitable that some parents and controls will refuse when asked at a later date, and in these cases, population controls should be used (page 15). If you have an accidental partial trio (e.g. a mother and index subjects, father later refuses), please speak to the DCC before recruiting a population control.

Do not recruit blood-related index subjects, e.g. if a father and son are both affected and can be recruited, but the mother cannot, you may only recruit *either* the father *or* the son as an index subject.

Once an index subject has been recruited to donate blood, a phenotyping form must be completed with the careful questioning of the patient and with the aid of a clinician. In some cases, (e.g. adopted index subjects), family IBD status will be unknown. This is simple for the *father*, *mother* and *second-degree relatives* sections, but for the siblings section, you must enter "0" for all fields. While this does not document the true answer ('unknown'), scientifically it is as accurate as for someone who does not have any siblings (neither has known affected siblings; neither has known unaffected siblings).

The *Macroscopic Disease Location*, *Surgery* and *Extra-intestinal Manifestations* sections must be completed by a clinician reviewing the patient's chart.

You may recruit more than one matched control for an index subject (subject A). This is an acceptable substitute for a second index subject (subject B) that has no matched control. When registering the two matched controls on the IBDGC website, be sure they are both linked to the control with whom they are matched (subject A).

You may also recruit *affected* siblings of the index subject if both parents of the index subject have also been recruited. These do not count towards your index subject or control accruals *per se*, but are useful for analyses. Do not recruit half-siblings, as they are considered second-degree relatives.

Following notification that Rutgers University Cell and DNA Repository (RUCDR) has received a subject or control blood sample, you may proceed with registering him/her on the IBDGC website. Index subjects must be registered <u>*prior to*</u> controls, siblings or parents. Therefore, (e.g.) if you are able to draw blood from the parents prior to the index subject/child, please do not register anyone until RUCDR has also received the index subject/child's blood.

Following registration on the IBDGC website, you may enter phenotype data using the IBDGC website interface.

Always be sure to check with index subject before discussing reasons for this study with controls and/or family members. An index subject may offer a control that is unaware of the patient's disease.

INFLAMMATORY BOWEL DISEASE (IBD) DEFINITIONS FOR DIAGNOSIS

The following diagnostic criteria are provided as guidelines to complete documentation on individuals with IBD enrolled in the NIDDK IBD Genetics Consortium:

Inflammatory Bowel Disease (IBD)

A) Symptoms including one or more of:
diarrhea, rectal bleeding, abdominal pain, fever, complicated perianal disease, extraintestinal manifestations, weight loss or failure to thrive
AND

B) Symptoms on two or more occasions separated by at least 8 weeks or ongoing symptoms of at least 6 weeks duration. When there has been a single episode of colitis (in some instances less then 6 weeks duration) resulting in colectomy and resolution of disease symptoms, pathology on the colectomy specimen should be consistent with idiopathic IBD and microbiology studies should be negative.
AND

C) One or more of the following providing *objective* evidence of inflammation:

Endoscopic: Mucosal edema, erythema, loss of normal submucosal vasculature, friability, ulceration, stricture formation, pseudopolyps, mucosal edema, erythema. *Where there are only minor changes (mucosal edema, erythema, loss of normal submucosal vasculature, friability) mucosal biopsies should have been done to confirm the presence of IBD.*

Radiologic: Mucosal thickening and/or nodularity, ulceration, stricture, pseudopolyps, fistula formation, pseudosacculation. Minor changes alone (mucosal thickening and/or nodularity) should not be sufficient to make a diagnosis of IBD.

Histologic: Mucosal erosion or ulceration, architectural changes of crypts, Paneth cell metaplasia (in colon), transmural inflammatory infiltrate*, fibrosis of muscularis propria*, noncaseating granuloma*

**Crohn's disease*

Individuals with IBD should be classified into one of three categories, based on most recent diagnosis:

Crohn's disease (CD)

1) Evidence of small intestinal inflammation with endoscopically, radiologically or histologically demonstrated ulcerations, fistulization, mucosal fissuring, nodularity or cobblestoning, stricture formation or histologically demonstrated transmural inflammation with or without granuloma formation.
2) Isolated esophageal, gastric or duodenal inflammation with the finding of non-caseating granuloma.

3) Colonic inflammation which is patchy (normal segments separating areas of inflammation, as described above) or associated with one or more of the following features: complete rectal sparing, multiple (>10) aphthoid ulcers, deep ulceration (into the muscularis propria), transmural inflammation, extensive fibrosis and wall thickening, fistulization, non-caseating granuloma.
4) The presence of complex suppurative perianal disease (i.e. more than a superficial fistula or uncomplicated superficial abscess).
5) If there are fewer than 10 aphthoid ulcers in the cecum (and the rest of the colon appears normal) in a patient with small bowel disease then this should be called small bowel disease only. Similarly, if the colon is normal except for the presence of a fistula extending from inflamed small bowel, the patient should be said to have small bowel disease alone. If the cecum is involved with ulcers larger than aphthoid ulcers or ulcers that are deep or if the involvement has resulted in deformity of the cecum this would be considered to be colonic involvement.

Ulcerative Colitis (UC)

1) Superficial inflammation and/or ulceration (involving only the mucosa and submucosa) of the colon which is continuous from the rectum extending proximally without skip lesions or complete rectal sparing (*N.B.* Relative rectal sparing is allowed for patients receiving topical rectal therapy).
2) No inflammation of the small intestine ("backwash ileitis" is allowed - non-stenosing superficial inflammation of the terminal ileal mucosa associated with severe pancolitis which resolves following medical or surgical treatment of the colitis).
3) No features of Crohn's disease listed above.

Indeterminate Colitis (IC)

1) *Confirmed* IBD by A, B and C above.
2) Physician unable to classify individual into either CD or UC based on above criteria and/or patient has features of both CD and UC with none of the features diagnostic of one or the other.

Crohn's Disease Phenotype Form

Registration Information

1. *Individual ID, Mother's ID, Father's ID and Family No*. are all optional. Each center may choose to assign these or disregard.
2. Gender.
3. *Date of Birth* is in format MM/DD/YYYY.
4. The NIDDK ID number is based on the sample label ID number, which is affixed to the form. The complete *Consortium ID* number is generated upon registration of subject using Consortium web interface; the last six digits will correspond to the NIDDK ID number.

Demographic and Diagnostic Information

1. *Hispanic/Latino* status ('Yes' / 'No' / 'Unknown') is self-reported.
2. *Jewish* status ('Yes' / 'No' / 'Unknown') is self-reported. Jewish, Ashkenazi status of each grandparent should be recorded.
3. *Race* is self-reported. Choose 'Other' under *Race* for multiracial individuals and fill in as required (up to 20 characters).
4. *Year of diagnosis* refers to the year in which a definitive diagnosis of IBD was made. In a case in which a patient is initially diagnosed with one form of IBD and subsequently has the diagnosis changed from one form of IBD to another form of IBD, the date of original diagnosis of IBD should be used. However, the most recent disease diagnosis (CD, UC or IC) should be used.
5. *Date of latest clinical exam/encounter* indicates the date of the most recent clinical, endoscopic, radiologic and/or pathologic records in the study participant's record, and is recorded as MM/DD/YYYY.
6. Family disease history as reported by the individual for all relatives listed. Relatives must have been diagnosed with IBD to qualify under 'CD', 'UC/IC' or 'IBD affected type unclear'. Does not require confirmation by relative or relative's medical chart. 'IBD Affected, type unclear' refers to a relative whom the individual knows has been diagnosed with IBD but isn't sure/cannot recall what type.
7. Determination of family type should include 1st and 2nd degree relative IBD affection as reported by the patient/participant. UC or IC in any 1st or 2nd degree relative would indicate mixed family type. *1st degree relatives* include parents, full siblings, and children. *2nd degree relatives* include grandparents, aunts/uncles and nieces/nephews and half-siblings.

Smoking History Prior to Diagnosis

1. Smoking is defined as smoking, on average, at least 1 cigarette daily for a period of at least 3 months prior to diagnosis. Pipe and cigar smoking are not included.
2. An *Ex-smoker* at diagnosis is defined as someone who had stopped smoking at least 4 weeks prior to diagnosis and was not smoking at diagnosis. If patient has had multiple episodes of quitting and starting smoking cigarettes indicate the year when first started and the year last quit.
3. If patient is a *Smoker* but dates of start and stop are unknown, leave dates blank.

4. If patient has never smoked indicate 'No', and leave *Year Started/Year Stopped* blank.
5. If smoking history is unknown, check 'Unknown', and leave *Year Started/Year Stopped* blank.
6. *No. of cigarettes per day*: indicate the number of cigarettes smoked daily. Where smoking amount has changed over time use the amount at diagnosis (if known). If not known, use the amount smoked at the date closest to the time of diagnosis. If Ex-smoker at diagnosis use the estimated mean number of cigarettes per day prior to quitting. If subject is a *Smoker* or *Ex-smoker* but the number of cigarettes per day is not known please indicate 'Unknown'. If patient had never smoked at diagnosis or smoking history is unknown please leave field empty.

Macroscopic Disease Location (check all that apply)-must be completed by a clinician
Must be confirmed by medical records. If region has not been examined for disease, enter 'Unknown' for that region. Check all areas of **macroscopic** disease at any time during the course of disease. If there are a few aphthoid ulcers in the cecum (and the rest of the colon appears normal) in a patient with small bowel disease then this should be called small bowel disease only. Similarly, if the colon is normal except for the presence of a fistula extending from inflamed small bowel, the patient should be said to have small bowel disease only. If the cecum is involved with ulcers larger than aphthoid ulcers or ulcers that are deep or if the involvement has resulted in deformity of the cecum this would be considered to be colonic involvement.

1. Location: Mucosal erythema, friability or granularity is not considered to be indicative of involvement. Mucosal ulceration, cobblestoning, stricturing or bowel wall thickening typically indicates involvement. Acceptable sources of information for classification are upper and lower endoscopy reports, barium X-rays, operative reports and pathology resection specimen reports. In cases where there is no information or missing information regarding evaluation of a portion of the GI tract, extent should be classified as 'Unknown' for that location. Operative descriptions of normal appearing small bowel or colon should not be used to classify 'No' for a site if that site has never been visualized by endoscopy or barium radiography. Perianal disease location is said to be present when an individual has a history of perianal or perineal abscess(es)and/or fistula, anal canal ulcers, anal stenosis or chronic edematous and violaceous skin tags. This does not include anal fissures or hemorrhoids.
2. CD Disease Behavior: *nonstricturing, nonpenetrating (B1), stricturing (B2) or penetrating (B3).* **Nonstricturing Nonpenetrating Disease (*B1*)** is defined as uncomplicated inflammatory disease without evidence of stricturing or penetrating disease. **Stricturing Disease (*B2*)** is defined as the occurrence of constant luminal narrowing demonstrated by radiologic, endoscopic, or surgical examination combined with prestenotic dilation and/or obstructive signs or symptoms but without evidence of penetrating disease. **Penetrating Disease (*B3*)** is defined as the occurrence of bowel perforation, intraabdominal fistulas, inflammatory masses and/or abscesses at any time in the course of the disease, and not secondary postoperative intra-abdominal complication. *Stricturing and penetrating should be classified B3.*

NB Perianal and rectovaginal fistula(s) do not count, by themselves, as 'penetrating fistulizing'.

Surgery-must be completed by a clinician

1. *Surgery for complication or treatment of CD*: must be confirmed by chart. If unconfirmed, then check 'No'. If no information, check 'Unknown'.

If Yes:

2. Bowel resection/strictureplasty includes:
   a. Resection or strictureplasty of stricturing disease
   b. Resection of disease that has been complicated by fistula or abscess
3. *Diversion* includes:
   a. Diversion procedures performed prior to definitive surgery such as resection
   b. Diversion procedures performed to allow healing of perineal disease
4. *Surgery for fistula/abscess* includes:
   a. Surgical fistulotomy
   b. Placement of a Seton
   c. Intestinal diversion to permit healing of perineal disease
   d. Surgical resection of a complicated fistula (e.g. enterovesical fistula)
   e. Surgical drainage of an abscess (e.g. perineal, intra-abdominal, iliopsoas)
   f. Percutaneous drainage of an intra-abdominal abscess that is followed by surgical resection of involved intestine
5. Surgery for fistula/abscess <u>does not</u> include:
   a. Simple incision and drainage of a perianal abscess performed using only local anesthetic
   b. Percutaneous drainage of intra-abdominal abscess without resection of involved intestine within 12 months
   c. Incidental resection of an enteroenteric fistula that occurs as part of an intestinal resection
6. *Year of first operation*: year of first **abdominal** surgery at <u>or</u> after diagnosis.
7. *No. of operations for abdominal disease:* (i.e. resection, strictureplasty, abscess drainage): a single operation may include two types of surgeries (e.g. a single operation during which both 'bowel resection' and 'abscess drainage' were performed).
8. *No. of operations for perineal disease (including diversions)*: a single operation may include two types of surgeries (e.g. a single surgery for perineal abscess and diversion)
9. *Appendectomy*: Should be noted as 'Yes' even if removal was part of another surgery. *If Yes indicate year*.

Extra-Intestinal Manifestations-must be completed by a clinician

Extraintestinal manifestations (EIM) should be documented in medical records (e.g. clinical note, radiology report, surgical report, pathology report).

1. *Joints*: pauciarticular (less than 5 joints involved with evidence of effusion or swelling – usually large joints - and associated with relapses of IBD); polyarticular (5 joints or more, symmetric involvement with effusion or swelling - usually small joint - runs a course independent of IBD often lasting many months); arthralgias (joint pains but no objective evidence of effusion or swelling)

are not indicative of joint "involvement" in the absence of other markers of active joint inflammation such as effusion or swelling.

a. *Large joint disease related to disease activity*: Fewer than 5 (usually large) joints related to disease activity
b. *Small joint unrelated to disease activity*: Five or more (usually small) joints unrelated to disease activity
c. *Ankylosing spondylitis*: requires radiologic documentation of typical findings of sacroiliac inflammation, narrowing or sclerosis and/or inflammation or fusion of vertebral bodies
d. *Sacro-iliitis*: also requires radiologic documentation of typical findings of sacroiliac inflammation, narrowing or sclerosis and/or inflammation or fusion of vertebral bodies
e. *Non-specific joint inflammation*: evidence of effusion or swelling but does not fit any of the above categories

2. Skin:
    a. *Erythema nodosum*: typically appear as raised, tender, red or violet subcutaneous nodules that are 1 to 5 cm in diameter. The nodules are most commonly located on the extensor surfaces of the extremities, particularly over the anterior tibial area
    b. *Pyoderma*: ulcerative disease of the skin. There may be one or multiple lesions. They occur most commonly on the legs, especially the pretibial area, but can develop in any area of the body, including the abdominal wall adjacent to the stoma after colectomy
3. Eyes:
    a. *Uveitis*: intraocular inflammation. Diagnosis requires documentation of typical findings. A slit lamp examination is preferable
    b. *Episcleritis*: Defined by the abrupt onset of mild inflammation of the episclera of the eye. Requires documentation of typical findings of localized inflammation (erythema, increased vascularity, nodularity) of the episcleral tissues
    c. *Undiagnosed ocular inflammation*: Where there has been eye inflammation but the presentation or findings have not been typical or where the nature of the inflammation cannot be classified based upon the available information
4. Liver:
    a. *Primary sclerosing cholangitis*: should be documented with typical dye cholangiographic or MRCP findings in someone with no other known causes of secondary cholangitis. Abnormal liver enzymes or liver biopsy alone are not sufficient evidence of sclerosing cholangitis

Ulcerative/Indeterminate Colitis (UC/IC) Phenotype Form

Registration Information

1. *Individual ID, Mother's ID, Father's ID and Family No.* are all optional. Each center may choose to assign these or disregard.
2. *Gender*.
3. *Date of Birth* is in format MM/DD/YYYY.
4. The NIDDK ID number is based on the sample label ID number, which is affixed to the form. The complete *Consortium ID* number is generated upon registration of subject using Consortium web interface; the last six digits will correspond to the NIDDK ID number.

Demographic and Diagnostic Information

1. *Hispanic/Latino* status ('Yes' / 'No' / 'Unknown') is self-reported.
2. *Jewish* status ('Yes' / 'No' / 'Unknown') is self-reported. Jewish, Ashkenazi status of each grandparent should be recorded.
3. *Race* is self-reported. Choose 'Other' under *Race* for multiracial individuals and fill in as required (up to 20 characters).
4. *Year of diagnosis* refers to the year in which a definitive diagnosis of IBD was made. In a case in which a patient is initially diagnosed with one form of IBD and subsequently has the diagnosis changed from one form of IBD to another form of IBD, the date of original diagnosis of IBD should be used. However, the most recent disease diagnosis (CD, UC or IC) should be used.
5. *Date of latest clinical exam/encounter* indicates the date of the most recent clinical, endoscopic, radiologic and/or pathologic records in the study participant's record, and is recorded as MM/DD/YYYY.
6. Family disease history as reported by the individual for all relatives listed. Relatives must have been diagnosed with IBD to qualify under 'CD', 'UC/IC' or 'IBD affected type unclear'. Does not require confirmation by relative or relative's medical chart. 'IBD Affected, type unclear' refers to a relative whom the individual knows has been diagnosed with IBD but isn't sure/cannot recall what type.
7. Determination of family type should include 1st and 2nd degree relative IBD affection as reported by the patient/participant. CD or IC in any 1st or 2nd degree relative would indicate mixed family type if proband has UC. CD or UC in any 1st or 2nd degree relative would indicate mixed family type if proband has IC. *1st degree relatives* include parents, full siblings, and children. *2nd degree relatives* include grandparents, aunts/uncles and nieces/nephews and half-siblings.

Smoking History Prior to Diagnosis

1. Smoking is defined as smoking, on average, at least 1 cigarette daily for a period of at least 3 months prior to diagnosis. Pipe and cigar smoking are not included.
2. An *Ex-smoker* at diagnosis is defined as someone who had stopped smoking at least 4 weeks prior to diagnosis and was not smoking at diagnosis. If patient has had multiple episodes of quitting and starting smoking cigarettes indicate the year when first started and the year last quit.
3. If patient is a *Smoker* but dates of start and stop are unknown, leave dates blank.

4. If patient has never smoked indicate 'No', and leave *Year Started/Year Stopped* blank.
5. If smoking history is unknown, check 'Unknown', and leave *Year Started/Year Stopped* blank.
6. *No. of cigarettes per day*: indicate the number of cigarettes smoked daily. Where smoking amount has changed over time use the amount at diagnosis (if known). If not known, use the amount smoked at the date closest to the time of diagnosis. If ex-smoker at diagnosis use the estimated mean number of cigarettes per day prior to quitting. If subject is a *Smoker* or *Ex-smoker* but the number of cigarettes per day is not known please indicate 'Unknown'. If patient had never smoked at diagnosis or smoking history is unknown please leave field empty.

Macroscopic Disease Location (check all that apply)-must be completed by a clinician Must be confirmed by chart. Check all areas of **macroscopic** disease that apply at any time during the course of disease. Acceptable sources of information for classification are colonoscopy reports, barium enemas, or colectomy gross pathology reports.

1. *Proctitis*: inflammation extending up to no further than 15 cm proximal to the anorectal junction
2. *Left-sided* (to splenic flexure): inflammation extending up to the splenic flexure. If this category is checked, so should *Proctitis*
3. *Extensive* (beyond splenic flexure): inflammation extending proximal to the splenic flexure. If this category is checked for a UC patient, *Proctitis* and *Left-sided* should be as well.
4. *Periappendiceal inflammation*: documented by colonoscopy with or without biopsy. Often accompanies *Extensive* disease.

Furthermore, patients with left-sided disease or proctitis and with an isolated patch of inflammation in the caecum should be recorded as having *Left-sided* disease only or *Proctitis* only, respectively.

Surgery-must be completed by a clinician

1. *Surgery for complication of UC*: must be confirmed by chart. If unconfirmed, then check 'No'. If no information, check 'Unknown'.

If Yes:

2. *Surgery for dysplasia/cancer*: When dysplasia or cancer is only found postoperatively on the surgical specimen but the indication for surgery was either acute fulminant or chronic continuous disease, dysplasia/cancer should not be included as an indication for surgery. However the presence of dysplasia/cancer should be indicated in the appropriate field (see #6).
3. *Surgery for chronic continuous disease*: should be indicated when there is neither an indication for fulminant colitis nor for dysplasia/cancer
4. *Surgery for acute fulminant disease*: fulminant colitis implies an acute or subacute onset of severe colitis (with or without signs of toxicity). This may occur over a period of 2 - 12 weeks in someone without a prior diagnosis of ulcerative colitis or in someone with a prior diagnosis of ulcerative colitis in whom the disease had been quiescent or stable prior to the fulminant exacerbation of disease activity.
5. *Year of surgery* (colectomy): year of first abdominal surgery at or after diagnosis.

6. *Diagnosis of dysplasia/cancer* (colorectal): If the patient has had disease less than 10 years or a negative surveillance colonoscopy then the answer is "no". If the patient has had disease more than 10 years and no surveillance (i.e. no biopsy after 10 years of disease or biopsy results not available) the answer is "unknown". If the patient has had confirmed dysplasia/cancer the answer is "yes".
7. *Appendectomy*: Should be noted as 'Yes' even if removal was part of another surgery. *If Yes indicate year*.

Extra-Intestinal Manifestations-must be completed by a clinician
Extraintestinal manifestations (EIM) should be documented in medical records (e.g. clinical note, radiology report, surgical report, pathology report).

1. *Joints*: pauciarticular (less than 5 joints involved with evidence of effusion or swelling – usually large joints - and associated with relapses of IBD); polyarticular (5 joints or more, symmetric involvement with effusion or swelling - usually small joint - runs a course independent of IBD often lasting many months); arthralgias (joint pains but no objective evidence of effusion or swelling) are not indicative of joint "involvement" in the absence of other markers of active joint inflammation such as effusion or swelling.
   a. *Large joint disease related to disease activity*: Fewer than 5 (usually large) joints related to disease activity
   b. *Small joint unrelated to disease activity*: Five or more (usually small) joints unrelated to disease activity
   c. *Ankylosing spondylitis*: requires radiologic documentation of typical findings of sacroiliac inflammation, narrowing or sclerosis and/or inflammation or fusion of vertebral bodies
   d. *Sacro-iliitis*: also requires radiologic documentation of typical findings of sacroiliac inflammation, narrowing or sclerosis and/or inflammation or fusion of vertebral bodies
   e. *Non-specific joint inflammation*: evidence of effusion or swelling but does not fit any of the above categories
2. *Skin*:
   a. *Erythema nodosum*: typically appear as raised, tender, red or violet subcutaneous nodules that are 1 to 5 cm in diameter. The nodules are most commonly located on the extensor surfaces of the extremities, particularly over the anterior tibial area
   b. *Pyoderma*: ulcerative disease of the skin. There may be one or multiple lesions. They occur most commonly on the legs, especially the pretibial area, but can develop in any area of the body, including the abdominal wall adjacent to the stoma after colectomy
2. Eyes:
   a. *Uveitis*: intraocular inflammation. Diagnosis requires documentation of typical findings. A slit lamp examination is preferable
   b. *Episcleritis*: Defined by the abrupt onset of mild inflammation of the episclera of the eye. Requires documentation of typical findings of localized inflammation (erythema, increased vascularity, nodularity) of the episcleral tissues

   c. *Undiagnosed ocular inflammation*: Where there has been eye inflammation but the presentation or findings have not been typical or where the nature of the inflammation cannot be classified based upon the available information

3. Liver:
   a. *Primary sclerosing cholangitis*: should be documented with typical dye cholangiographic or MRCP findings in someone with no other known causes of secondary cholangitis. Abnormal liver enzymes or liver biopsy alone are not sufficient evidence of sclerosing cholangitis

Unaffected Phenotype Form for controls

Registration Information

1. *Individual ID* and *Pedigree ID* are optional. Each center may choose to assign these or disregard.
2. *Gender*.
3. *Date of Birth* is in format MM/DD/YYY.
4. The NIDDK ID number is based on the sample label ID number, affixed to the form. The complete *Consortium ID* number is generated upon registration of subject using Consortium web interface; the last six digits will correspond to NIDDK ID number.
5. *Relationship to Proband*: must be one of i) parent, ii) spouse/domestic partner, iii) friend* or iv) population control*. Categories ii and iii must also fit checklist profile fully. Domestic partner refers to a non-friend person, not married to but cohabitating with, the proband. Category iv must fulfill requirements below (6). You may also recruit full siblings, if he/she is affected.
6. *Population Control*: Must be linked to an index subject. Must match that index subject by i) race, ii) ethnicity (Jewish and Hispanic/Latino status), and 3) age: must be within 10 years of the index subject. The population control must be recruited at the same GRC (and satellite center if applicable) as the index subject.
7. *Control Checklist*: *Same race/ethnicity as index subject* is as self-reported. Matched Jewish ethnicity must also match Ashkenazi status (e.g. if proband has 2-4 Ashkenazi Jewish grandparents, control must have any of 2, 3 or 4 Ashkenazi grandparents. If proband has only 1 Ashkenazi grandparent but all are Jewish, control must have 1 or 0 Ashkenazi grandparents, but 2 or more must be Jewish). *No family history of IBD* refers to 1st and 2nd degree relatives (parents, siblings, offspring, aunts/uncles, grandparents, nieces/nephews).

Demographic Information

1. *Hispanic/Latino* status ('Yes' / 'No' / 'Unknown') is self-reported.
2. *Jewish* status ('Yes' / 'No' / 'Unknown') is self-reported. Jewish, Ashkenazi status of each grandparent should be recorded.
3. *Race* is based on self-reporting. Choose 'Other' under *Race* for multiracial individuals and fill in as required (up to 20 characters).
4. If *duration of cohabitation* of spouse/domestic partner is less than 1 year, indicate '0'.

Smoking History

1. Indicate if control is *Current smoker, Ex-smoker, Non-smoker* or *Unknown*.
2. If control has smoked less than 100 cigarettes in his/her lifetime, he/she is considered to be a non-smoker.
3. If control has had multiple episodes of quitting and starting smoking cigarettes indicate the year when first started and the year last quit, unless currently smoking.
4. If *Current smoker*, leave *Year stopped* blank.

Surgery

1. Indicate 'Yes', 'No' or 'Unknown' and enter year of appendectomy if known.

• If index subject is under 18, non-trio controls may be between the ages of 18-24years, with no smoking history.

Glossary

Abscess:
A localized collection of pus in part of the body formed by tissue disintegration and surrounded by an inflamed area.
Ankylosing Spondylitis:
Arthritis of the axial skeleton manifested by back pain and progressive stiffness of the spine.
B1:
CD Disease Behavior, nonstricturing, nonpenetrating. Defined as uncomplicated inflammatory disease without evidence of stricturing or penetrating disease.
B2:
CD Disease Behavior, stricturing. Defined as the occurrence of constant luminal narrowing demonstrated by radiologic, endoscopic, or surgical examination combined with prestenotic dilation and/or obstructive signs or symptoms but without evidence of penetrating disease.
B3:
CD Disease Behavior, penetrating. Defined as the occurrence of bowel perforation, intraabdominal fistulas, inflammatory masses and/or abscesses at any time in the course of the disease, and not secondary postoperative intra-abdominal complication. NB *Perianal and rectovaginal fistula(s) do not count, by themselves, as 'penetrating fistulizing'.*
Cecum:
The large blind pouch forming the beginning of the large intestine. Also called blind gut.
Endoscopy:
Examination of the interior of a hollow body organ by use of an endoscope.
Episcleritis:
Defined by the abrupt onset of mild inflammation of the episclera of the eye. Requires documentation of typical findings of localized inflammation (erythema, increased vascularity, nodularity) of the episcleral tissues. The episclera is a highly vascular connective tissue that is superficial to the sclera of the eye.
Erythema Nodosum:
Typically appear as raised, tender, red or violet subcutaneous nodules that are 1 to 5 cm in diameter. The nodules are most commonly located on the extensor surfaces of the extremities, particularly over the anterior tibial area.

Ex-smoker:
Someone who has smoked prior to diagnosis, but was not smoking at time of diagnosis.
Fistula:
An abnormal duct or passage resulting from injury, disease, or a congenital disorder that connects an abscess, cavity, or hollow organ to the body surface or to another hollow organ.
Macroscopic:
Large enough to be perceived or examined without microscopy.
Non-smoker:
A person who has never smoked, at time of diagnosis.

Non-specific joint inflammation:
Evidence of effusion or swelling but does not fit any of the other categories.
Percutaneous Drainage:
Drainage performed through the skin or accomplished by a needle.
Population Control:
Must be linked to an index subject. Must match that index subject by i) race, ii) ethnicity (Jewish and Hispanic/Latino status), and 3) age: must be within 10 years of the index subject. The population control must be recruited at the same GRC (and satellite center if applicable) as the index subject.
Primary Sclerosing cholangitis:
A chronic progressive disorder of unknown etiology, characterized by inflammation, fibrosis, and stricturing of medium size and large ducts in the intrahepatic and extrahepatic biliary tree (bile ducts in- and outside the liver).
Pyoderma:
Ulcerative disease of the skin. There may be one or multiple lesions. They occur most commonly on the legs, especially the pretibial area, but can develop in any area of the body, including the abdominal wall adjacent to the stoma after colectomy.
Resection:
Excision of a portion or all of an organ or other structure.
Sacro-iliitis:
Arthritis of the sacroiliac joint.
Seton:
One or more threads or horsehairs or a strip of linen introduced beneath the skin by a knife or needle to provide drainage.
Smoker:
Someone smoking at time of diagnosis.
Strictureplasty:
Surgical procedure for widening a structured segment of intestine that involves incision and closure in opposing directions.
Undiagnosed ocular inflammation:
Where there has been eye inflammation but the presentation or findings have not been typical or where the nature of the inflammation cannot be classified based upon the available information.
Uveitis:
Intraocular inflammation. Diagnosis requires documentation of typical findings. A slit lamp examination is preferable.