Council on Dairy Cattle Breeding CDCB Genomic Nominators Workshop 5/17/2017

Kaori Tokuhisa, CDCB Genomic Data Analyst



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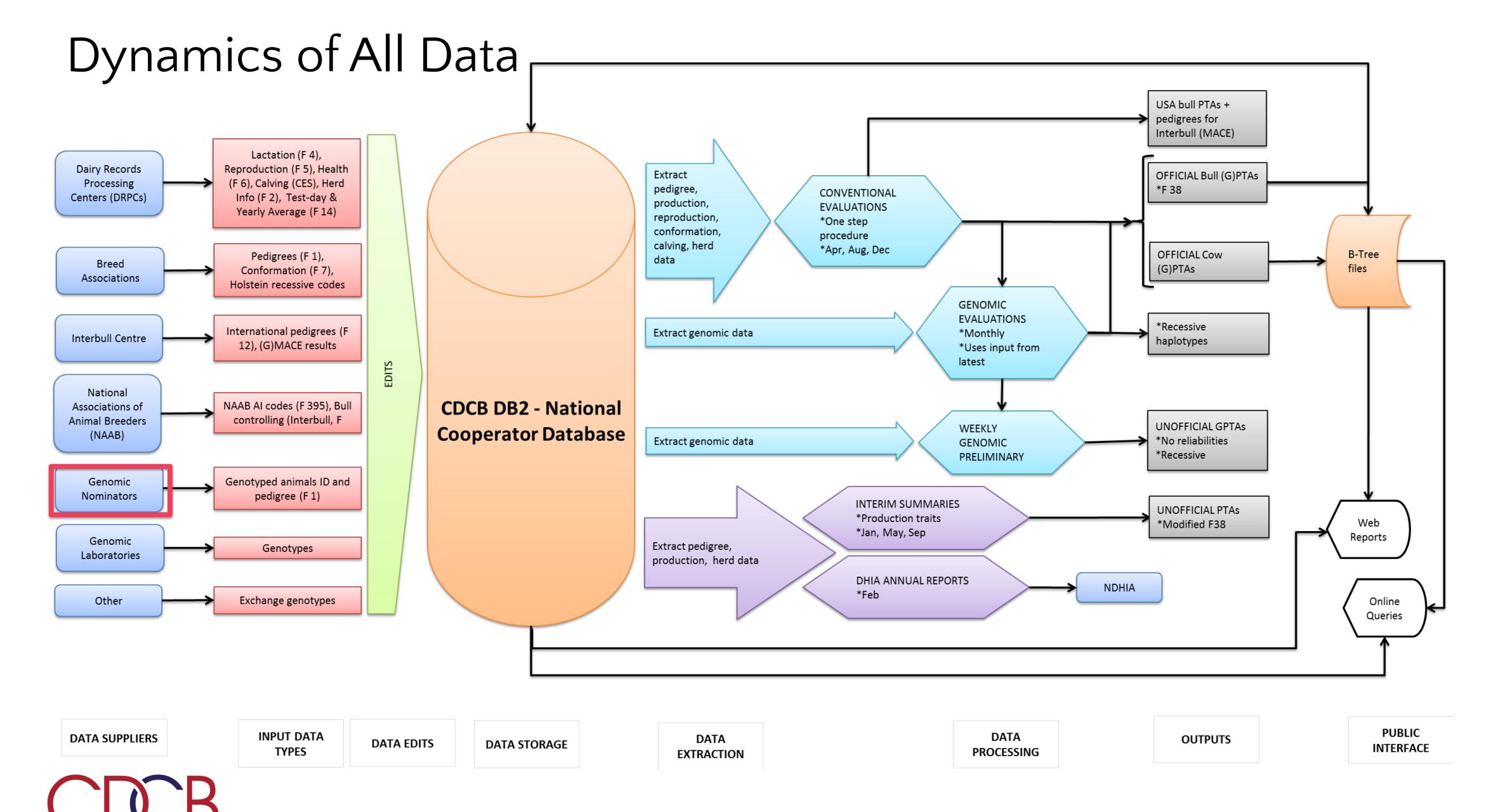
1. Introduction

- Kaori Tokuhisa (Genomic Data Analyst, 2 years at CDCB)
 - Genomic data loading
 - -Certification of Nominators and laboratories
 - -Quality control
 - -Customer service
 - -Nominator QC audit (<-New, Joao will present this in the afternoon)
- Worked at Genus (ABS/PIC) for 3 years as a quantitative data analyst in a research team
- Graduated from UGA under Dr. Misztal



2. Data Flow





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Data Exchange between Nominator and CDCB in FTP area ("in" directory)

Pedigree	Nomination
YYYYMMDD.1.X	YYYYMMDD.1GX
(format1)	(format1G)

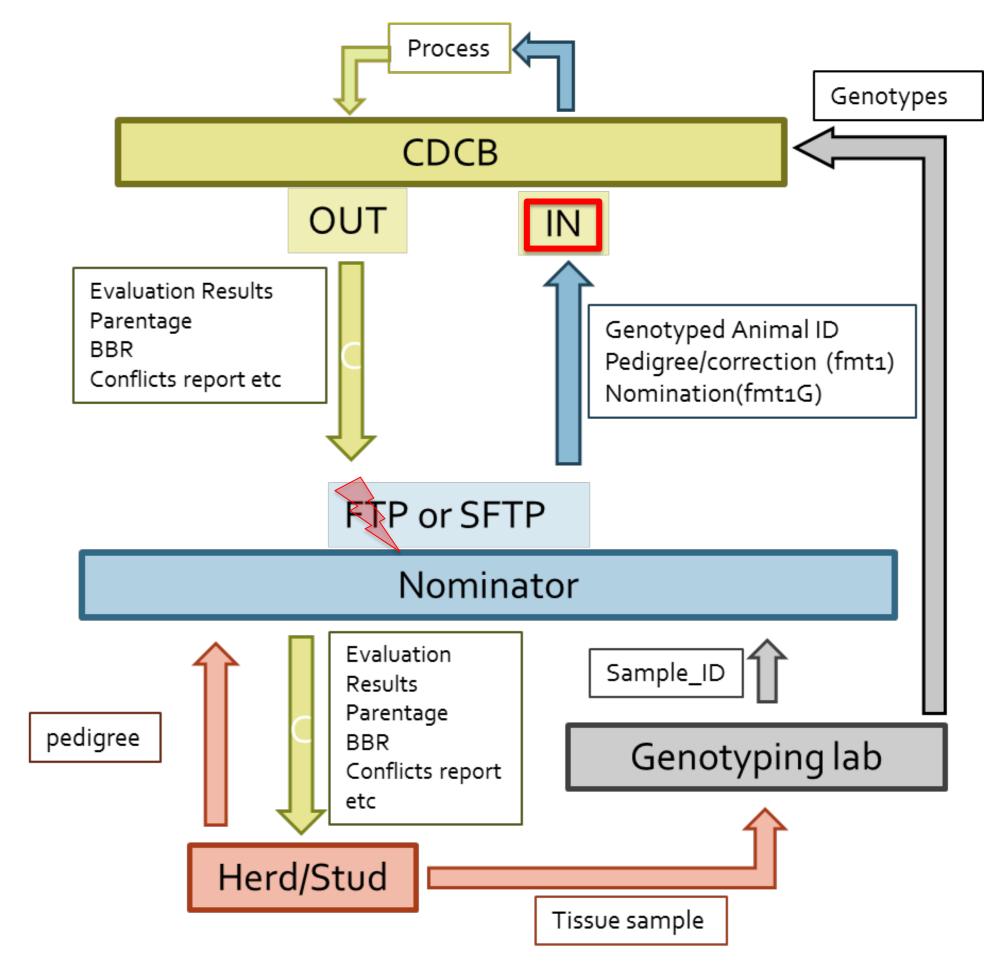
https://www.uscdcb.com/CF-RCS/GetRCS.cfm?DocType=formats&DocName=fmt1.html

YYYY=year of the submission

MM = Month of the submission

DD = Date of the submission

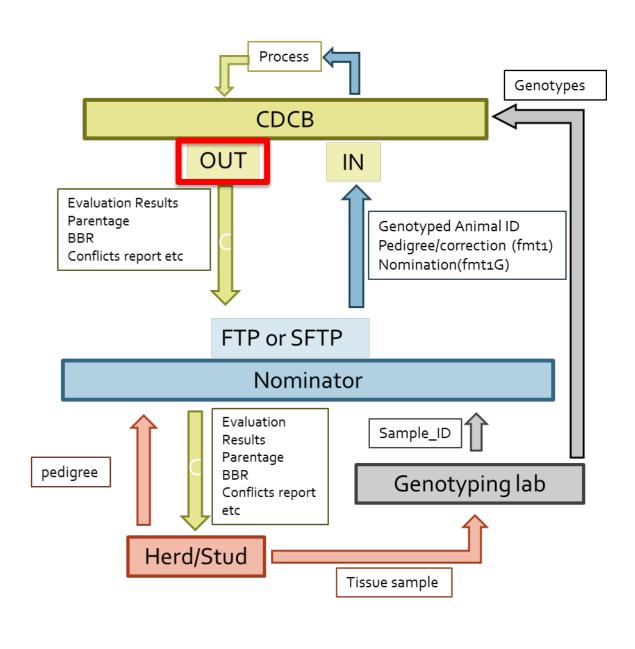
X = Any Alphabets or integers





Data Exchange between Nominator and CDCB in FTP area ("out" directory)

Weekly Run	Monthly Run	Tri-Annual Run (April, Aug, Dec)	Quality Control	Update job (-o)
BB_young_Pub_YYYYMMD D_TIME.csv (Young bulls PTAs to be published-BA only)	BB_NOM_YYMM.csv (PTAs nominated by NOM)	BB105.zip (Cow's PTAs-BA only/available through web query)	YYYYMMDD.1(G)Ex (fmt1(G) error/conflict)- when fmt1(G) is submitted	NOM_Parentage_YYYYMM DD_TIMESTAMP.csv (parentage update)
BB_Cow_PTA_YYYYMMDD. csv (Cow's PTAs-BA only)	BB_young_Pub_YYMM.csv (Young Bulls' PTAs to be published-BA only)	BB38.zip (Bull's PTAs-BA only/available through web query)	Notify.YYYYMMDD.1(G)X.tx t (notify file for fmt1(G)))-when fmt1(G) is submitted	NOM_PGS_unlikely_YYYYM MDD.csv (GS unlikely)
BB_NOM_YYYYMMDD.csv (PTAs nominated by NOM)	BB_NOM.BBRdata.YYMM.c sv(BBR for monthly)		Lab_YYYYMMDDXX.zip (nominator report, genomic conflicts, parentage, no nomination)	
BB_NOM.BBRdata.YYYYMM DD.csv (BBR)	NOM_Check_Fee_Code_Y YMM.csv			
BB_NOM_YYYYMMDD_hapl o_data.csv (haplotype)	BB_NOM_YYMM_haplo_da ta.csv			





BB=Breed (ex.AY,BS,GU,HO,JE,MS) YY(YY)= 2 or 4digits year (ex. 16, 2016) MM=2 digits month (ex. 04 for April)

LAB= Name of genotyping lab X = Any Alphabets or integers NOM= Nominator ID

3. Nomination



How to Nominate Animals

•CDCB expects a nomination to be completed **before** receiving the genotype from the lab

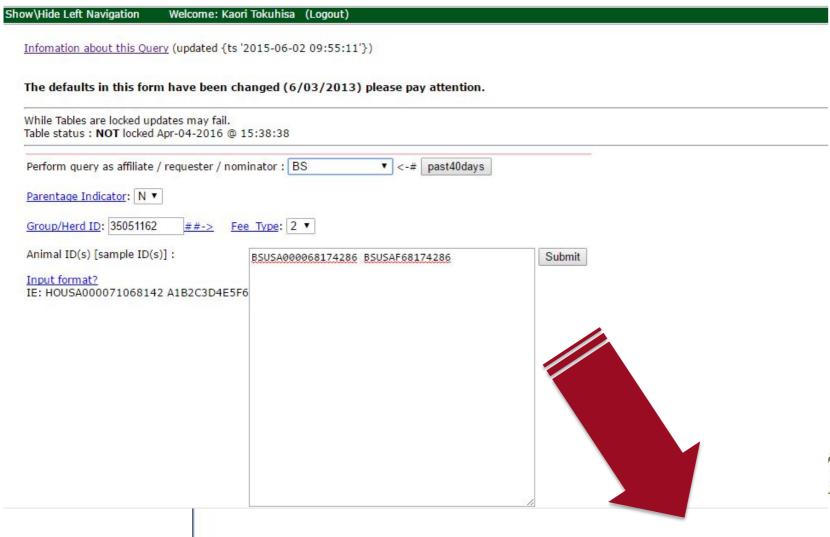
2 ways to nominate animals

- Nominate animals through CDCB Web query (https://www.uscdcb.com/CF-queries/Nom2.cfm)
- 2. Nominate animals by submitting format1G file to CDCB (https://www.uscdcb.com/CF-RCS/GetRCS.cfm?DocType=formats&DocName=fmt1.html)



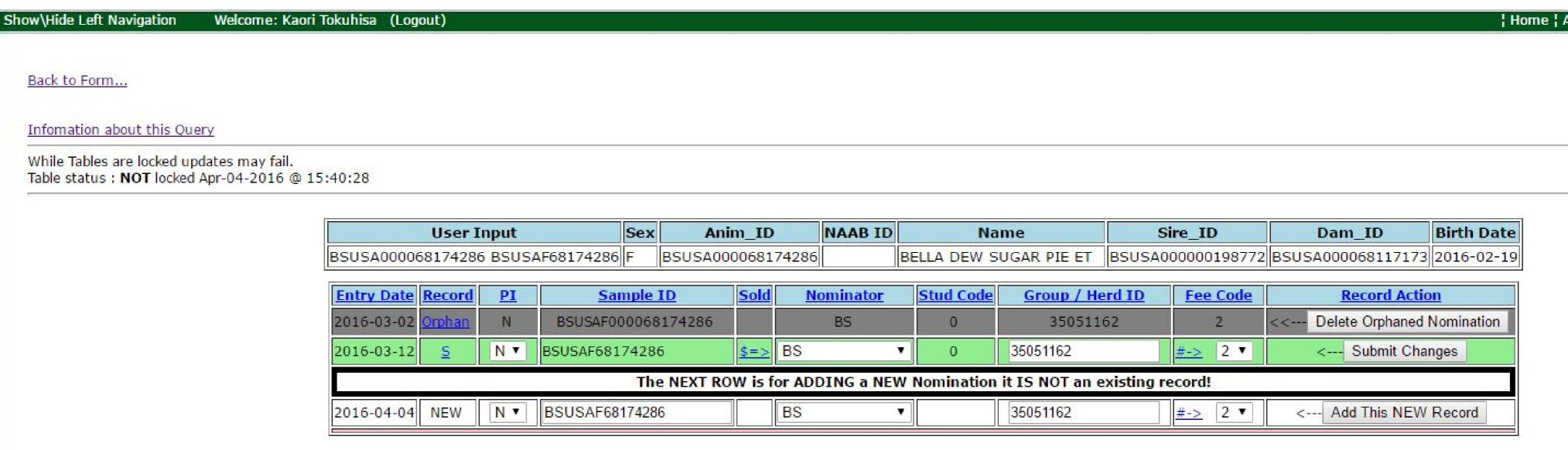
Nomination through Web Query

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*Web query only works when we already have the animal's pedigree in our system or when you know that the animal has been registered at an external organization, such as breed associations or Interbull.

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Nomination (submission of Format1G through (S)FTP)

OFBSUSA000068174286BSUSA000000198772BSUSA000068117173A1B2C3D4E5F6 20160219B20160312G013HR000000BELLA DEW SUGAR PIE ET 35051162N2 Process YYYYMMDD.1GX Genotypes **CDCB** OUT IN **Evaluation Results** Parentage Genotyped Animal ID BBR Pedigree/correction (fmt1) Conflicts report etc Nomination(fmt1G) FTP or SFTP Nominator Evaluation Sample_ID Results Parentage pedigree BBR Genotyping lab Conflicts report etc Herd/Stud Tissue sample



4. Common Reasons Why You May Not Receive Genomic Evaluations

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How to Correct Them



- 1. Genotype was not usable due to a conflict, low call rate, being a crossbred (PI="B")
- 2. The genotype became usable after the genotypes were extracted for the evaluation
- 3. The breed of evaluation is not among those we generate evaluations for
- 4. The animal's genotype conflicted its imputed dam
- 5. The fee code is "N (No fee paid)" or "H (Historic)"
- 6. The bull has semen marketed and its not a traditional evaluation release
- 7. The owner of the bull is not located in the US, so the evaluation is not public
- 8. The genotype is designated parentage verification only (PI="P")
- 9. The bull is foreign, over 15month of age and no AI service fee has been paid
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10. Cannot find evaluation results

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10. Cannot find evaluation results

Where to find a file that contains genomic conflicts?

 In the out directory, a zip file is placed once Lab load a batch of genotype data to our database:

LAB_YYYYMMDDXX.NOM.zip (ex. GSek_20160426A1.ABS.zip)

Biogenesys
Genetic Visions
GeneSeek
Weatherbys
VHL
Zoetis
BioG
Gvis
GVis
GSek
Weab
VHL

Zoetis

BioG

VVis
GVis
GVis
GSek

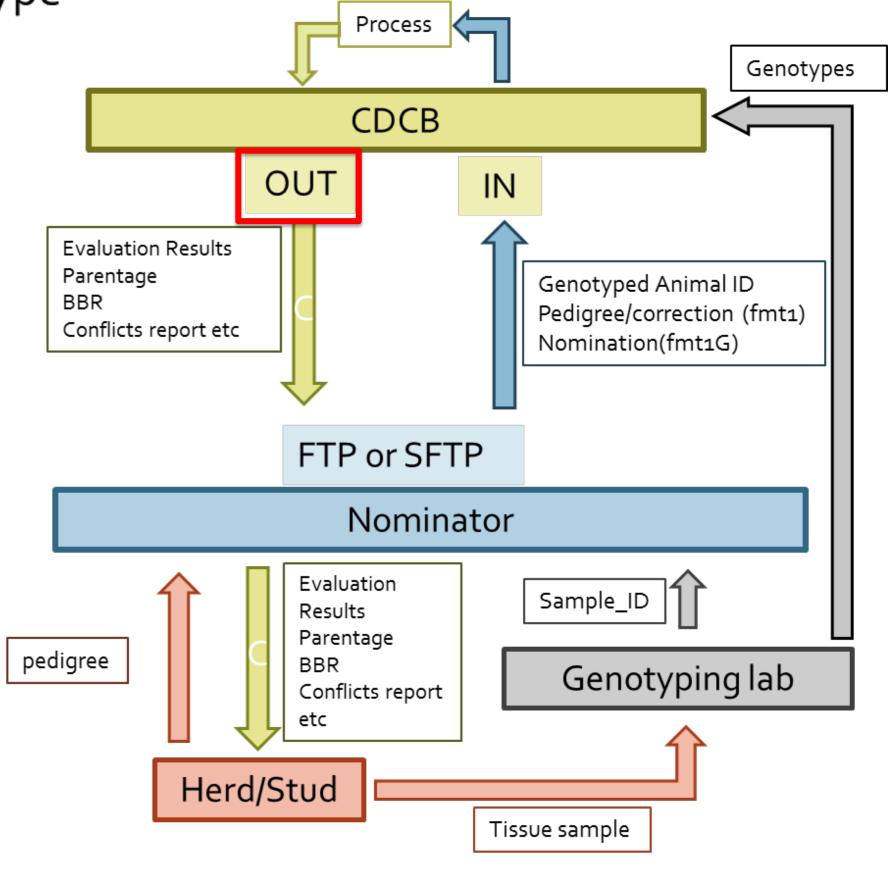
Weab

VHL

Zoet

And in the zip file, there are files below

File Name	Description of file
NOM_Nominator_Report.csv	Numbers of error/conflict
NOM_Genomic_conflicts.htm	Animal with error code (web version)
NOM_Genotype_Conflicts.csv	Animal with error code (in csv)
NOM_Parentage.csv	parentage
NOM_LABCHIPYYYYMMDDX_No_Nomination.csv	Animals with missing nomination





You can also find individual's genomic error(s) in an online query called Genotype Query(30 SNP)

Genomic Error Code Documentation

NOM_Genotype_Conflicts.csv (in csv format)

- You may notice that there are 6 places for ID and code.
- -This is because multiple animals and conflicts may be involved in the record, such as error related to parents, siblings, grandparents.

ID1-6: ID involved in the errors/conflicts

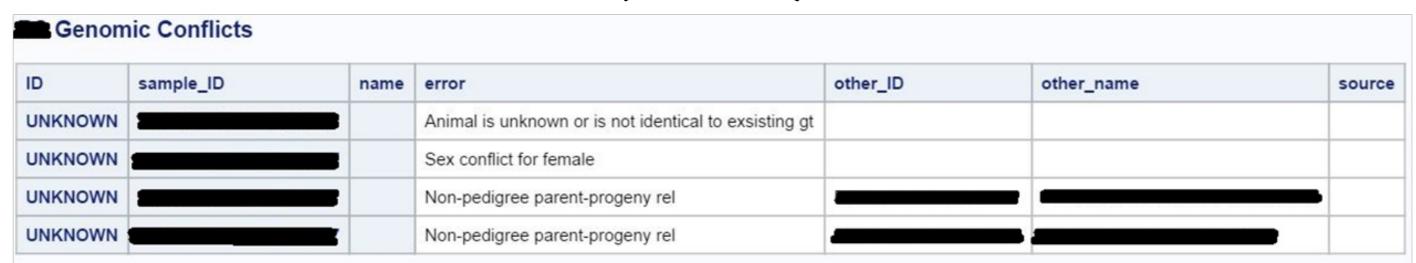
Code1-6: Error code that describes the issue that was detected by their genotypes

Description of genomic errors (https://www.uscdcb.com/formats/gen_error.html)

N2 Sex conflict for female

O₃ Non-pedigree parent relationships /Discovered parent

NOM_Genomic_conflicts.htm (web ver)





Frequently asked Genomic Error Questions

- a. Genotype is low call in autosomal chromosomes (M3)
 - a. Threshold: 90%
 - b. Re-genotype is required.
- b. Genotypes is low call in X-chromosomes (M4)
 - a. Threshold: 80%
 - b. Re-genotype is required.
- c. Sex conflict for males and females (N1&N2)
 - a. Heterozygous calls in X and no call in Y (Male) -or- No Heterozygous call in X but some calls in Y in Female.
 - b. Wrong sample (most of the time) or bad quality of DNA (re-genotype)
- d. Unreliable genotype due to male with sufficient Y SNP and excessive heterozygous SNPs on X chromosome (Q3)
 - a. Poor quality sample (most of the times), XXY karyotype (not practical)
- e. Bull genotype has more heterozygous X-specific SNP than explainable as genotyping errors (Q4)
 - a. Notification only genotype not excluded.
- f. "Sire conflict / dam conflict" vs "Unreliable genotype due to high parent progeny conflict" (N3&N4 vs O8)
 - a. "conflict" We are confident that there is conflicts in the parent-progeny relationship (mostly due to miss-identification/assignment)
 - b. "unreliable" There are more SNP conflict than the one that we see in normal parent-progeny relationships (maybe due to genotyping errors)

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Evaluation Schedule

Weekly evaluation

- Only animals with first genotype
- Unofficial GPTAs
- Release: Tuesdays at 8am

Monthly evaluation

- All genotyped animals
- Data due (genotype): Online
- Release: First Tuesday of the month at 8.30am

Traditional (triannual) evaluation

- April, August, December
- Traditional and Genomic evaluations
- Data due and release dates: Online



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Breed Conflicts





- Crossbred indicated in pedigree + genotype or mismatched breed between pedigree and genotype
- The system checks that the breed indicated on the sample is the breed with the fewest unlikely breed specific alleles (ranges from 216 to 672 SNPs)

	BS/HO/JE	AY/GU
#SNP > 35,000	80 SNPs	7 SNPs
#SNP < 35,000	6 SNPs	7 SNPs

Under revision

 If you get breed conflict or PI=B, it means that either the animal is not a breed that we evaluate, or this animal is crossbred, therefore this animal will be excluded from evaluations



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4. conflicts with the genotype of the imputed dam

- · Recently, the nominators have begun to be notified when there is a conflict with the genotype of the imputed dam.
- Query available to see the conflicts (Affiliate specific genotype report)
- Genotypes with these conflicts do not change the usability of the genotype, but they will be excluded from evaluations
- Pedigree correction will be necessary in order to resolve the conflicts



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9. The bull is foreign, over 15month of age and no AI service fee has been paid

-Foreign genotyped males will receive a genomic evaluation monthly up through 15 months of age with the genomic evaluation only provided to the nominator.

-Foreign males must pay the AI Service Fee to get a genomic evaluation publically released past 15 months of age



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10. Cannot find evaluation results

- When you search for evaluation results for specific IDs, please make sure you have the correct ID
 - the animal ID should consist of :

 2digits breed code + 3 digits country code (+ 1 optional sex code)+ 12 digits ID = 17 (+1) digits
- If the animal is cross referenced, you should look for preferred ID, not cross referenced ID (secondary ID)
- Check all the factors that might be preventing you from receiving the results



5. Nomination and Data Correction Using Web Query



Web Query Tools

COUNCIL ON DAIRY CATTLE BREEDING Home About Help Contact Us En Espanol Show\Hide Left Navigation Welcome: Kaori Tokuhisa (Logout) How Do I? This query is used to ADD/REMOVE/UPDATE nominations and UPDATE genotype information. CDCB-Nomination Q Genotype reports based on requester affiliate specific genotype reports Check FMT1 records. Check FMT1 records Get 116 parentage SNP Get 116 parentage SNP for a list of animal IDs This is used to show (and fix) the usability/error status of received genotypes. Genotype Query(30 SNP) This is the CDCB Fee (by herdcode) Query GT Fee Retrieve Parentage Validation Record parentage.cfm This is for correcting bad genotype to animal assignments. Genotype Move/Swap APP Provides herd code and CDCB Fee for specified animal ID



CDCB-Nomination_Q

- -submission of format1
- -Nomination
- -Add, remove, update nomination status

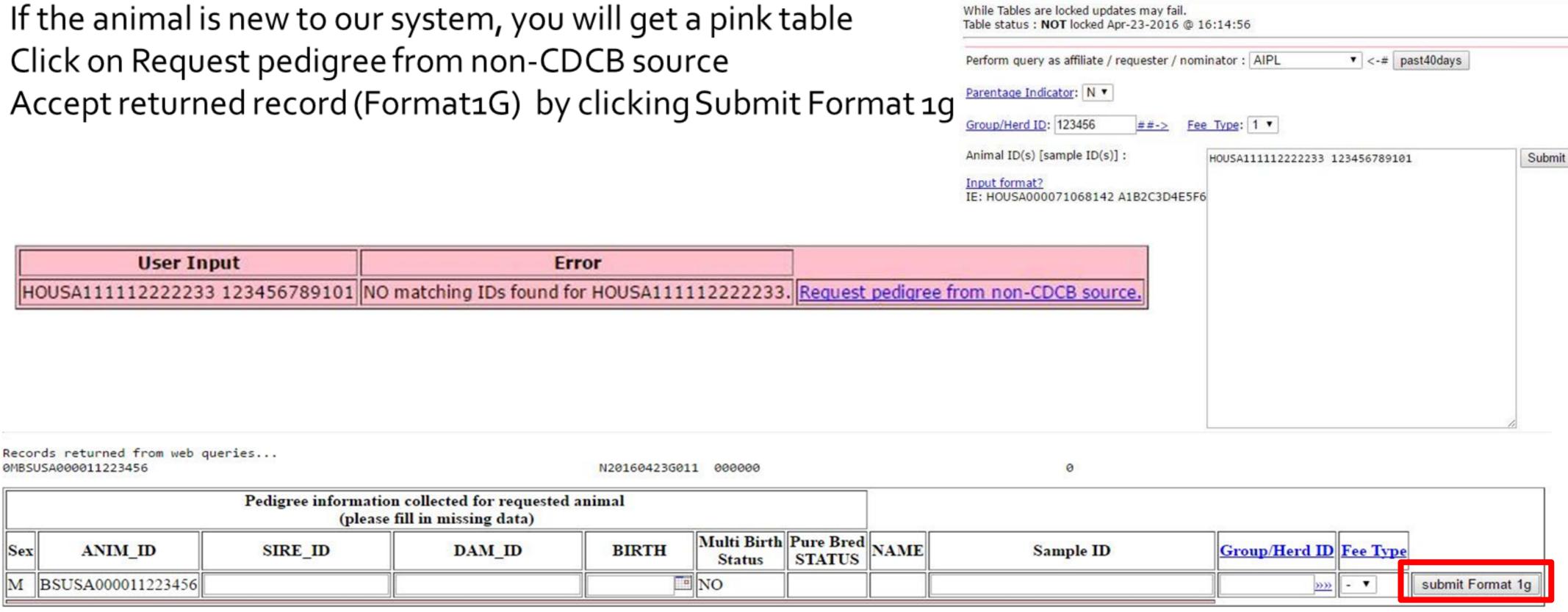
Reminder: There are 2 ways to nominate animals, as discussed earlier

- Nominate animals through CDCB Web query (https://www.uscdcb.com/CF-queries/Nom2.cfm)
- Nominate animals by submitting format1G file to CDCB (https://www.uscdcb.com/CF-RCS/GetRCS.cfm?DocType=formats&DocName=fmt1.html)



Submission of Format1G for new animal through Web query

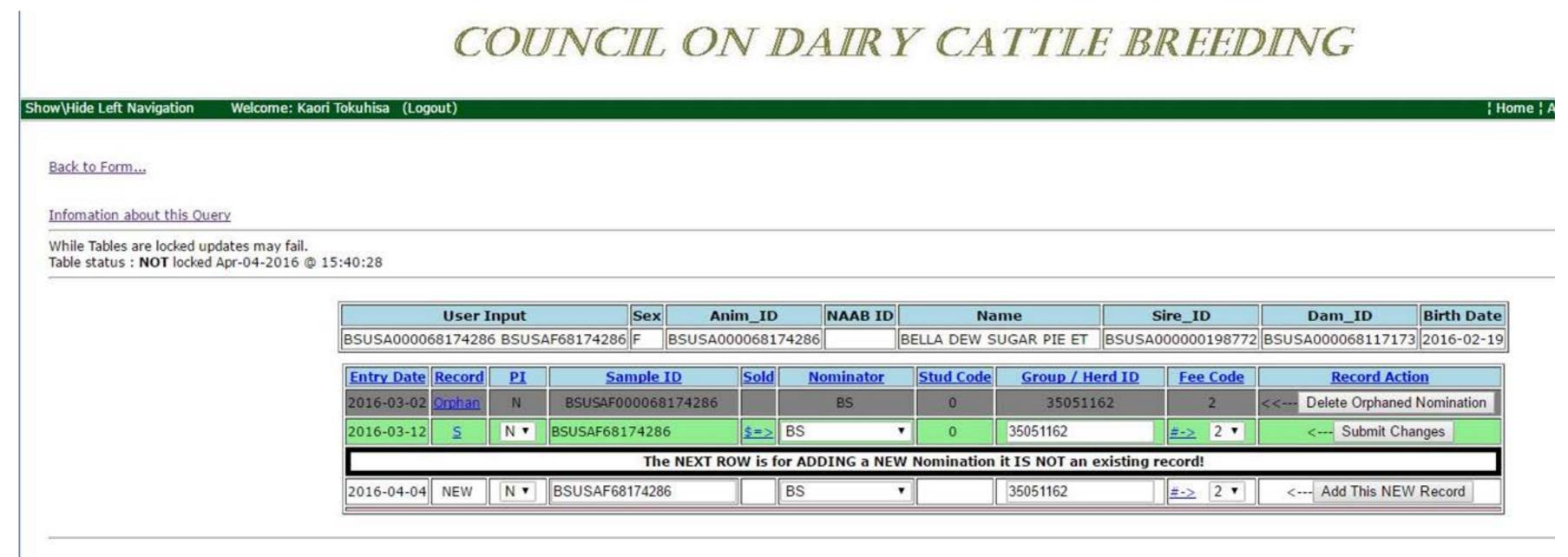
- Open nomination query and put new animal and the sample ID just like normal nomination
- Click submission
- If the animal is new to our system, you will get a pink table
- Click on Request pedigree from non-CDCB source
- 5. Accept returned record (Format1G) by clicking Submit Format 1g





Change nomination status - How to change requester ID

- The query will display pedigree information (to confirm animal identification), all nominations, and stored genotypes (including pending genotype changes) for the given animal(s).
- To change the requester_id to one that is NOT yours:
 Click the '\$=>' link in the 'Sold' column, to populate the 'Nominator' drop down in this row with all known Requester_IDs. An Email will get sent to the new nominator, to notify them of this change.





Affiliate specific genotype reports

1. Lists genotypes with fee code=N loaded in the past 6 months

• Fee code =N indicates that the fee code has not been assigned to the animal (No evaluation will be released)

2. Fee codes for genotypes loaded since the last invoice

Fee code for each animal that you will be receiving invoice for

3. Lists parentage only genotypes since the previous genomic run

- Parentage only genotypes are not evaluated in our genomic evaluation
- Animals will not get evaluated until the PI becomes "N"

Parentage Validation Record

Sire/Dam Status Code: Genotype Usability Indicator: Parentage Indicator: Y - Confirmed N - No restrictions N - Not usable P - Parentage Only H - Conflict based on MGS test (dam only) L - Low Call Rate R - Research Only

M – Multiple (usable)

U - Unreliable (not usable)

U – Unable to test (no genotype / blank pedigree)

MGS Status Code:

N - Conflict

Y - Likely

U - Unable to test (no genotype / blank pedigree)

N - Unlikely

H – Unlikely; MGS suggestion based on haplotype test

S – Unlikely; Dam's sire is wrong based on haplotype test

X - Unlikely; No MGS suggestion

Animal ID	Sample ID	Chip Type	Sire ID	Sire Status Code	Suggested Sire	Dam ID	Dam Status Code	Suggested Dam	MGS Status Code	MGS Sugg1-4	MGS Stat1-4	Usability Indicator	Parentage Indicator	Date
HOUSAF0001 23456789	HAU01234 56A-01	50K	HOUSAM0001 23456789	Y,N,U	HOUSAM0009 87654321	HOUSAF0001 23456789	Y,N,U	HOUSAF0009 87654321	Y,N,U,I,H,S,X	HOUSAM0 001234567 89	8	Y,N,L,M,U	N,P,R,B	20111018

All others – <16.0 (50K and HD) <22.0 (3K and LD) are likely; Lower values = more relationship to genotyped animal. Separation between suggested animals is

4. Reports missing animal ID for a requester

- This report indicates genotypes that has been loaded to our database, but no animal IDs are associated
- Only the genotype is stored on our database



B – Breed exclusion from genomic evaluation

(AY, GU, MS & Crossbreds)

Affiliate specific genotype reports 2

5. Conflicts for genotypes loaded in the past 45 days

• Genotypes with conflicts will be unusable for the evaluation until it gets resolved and status becomes "usable"

6. Check for missing pedigree of animals nominated in the past 75 days

- Shows animal IDs that has been nominated with unknown parents or unknown grandparents and their genotypes has not arrived to CDCB yet.
- Can be used to find miss reported sireID

7. List conflicting genotypes within animal (negative keys)

• Genotypes with negative key should be re-assigned to the correct animal, if possible

8. Animals with genotypes that conflict with imputed dam genotypes

• You can find which sample_ID (genotype) is having conflicts with which Dam from this query

9. Parentage verification records for genotypes loaded in the past 45 days

 Contains all genotyped animals' parentage comfirmations/suggestions that came into our system in the past 45 days



Genotype Query (30 SNPs)

• This is used to show (and fix) the usability/error status of received genotypes



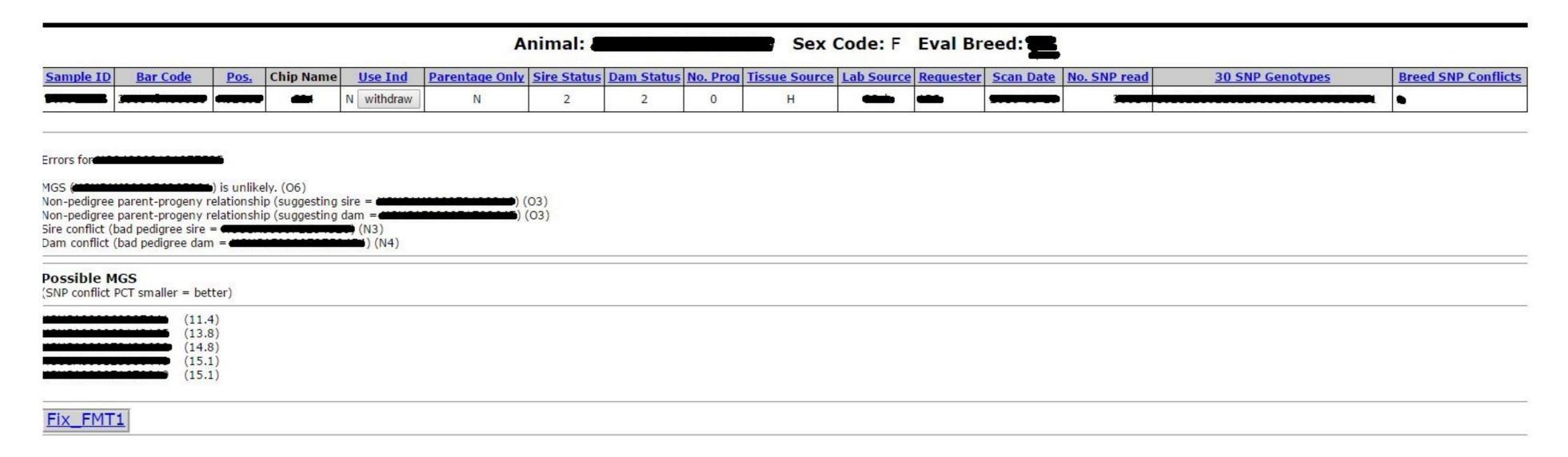
FMT1 Records: ANIM Sire Dam Alias/Clone Ped_Veri Rec Multi Birth Reg Future r Proc_Date(YYYYMMDD) Name(30) Future Use ID17 ID17 ID17 ID17 (YYYYMMDD) Ver Code Stat Type Code current CDCB pedigree data 00000000000 1 1 000000 sugestions are based on genotypes and other data such as current sire/dam/animal pedigree birthdates, sample labeling, etc... 00000000000 1 1 000000 User Input 000000 00000000000 Submit Changes



Return to 'Genotype Status' query

How to withdraw genotypes

If the genotype belongs to one of your affiliate/nominator/requester ID(s) and has a Usability Indicator of N,L, or U, there should be a 'withdraw' button in the Use Ind column at Genotype Query(30 SNP).





GT Fee

• This application searches fee code, based on given "HERD ID"

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nisa (Logout)				
Enter herd ID nun	mber :			
35280016				
(e.g., 35280016) Submit				
	data from the Dec,201	5 run		
Herd Kind 35280016 1 Tota	d of Participation			



Parentage.cfm

- This query outputs parentage information in excel sheet for specific animals
- Animal ID, sample information, sire, dam, grand parents etc.

Parentage Validation Record

Sire/Dam Status Code:	Genotype Usability Indicator:	Parentage Indicator:
Y – Confirmed	Y – Usable	N – No restrictions
N – Conflict	N – Not usable	P – Parentage Only
H - Conflict based on MGS test (dam only)	L – Low Call Rate	R - Research Only
U - Unable to test (no genotype / blank pedigree)	M - Multiple (usable)	B - Breed exclusion from genomic evaluation
MGS Status Code:	U - Unreliable (not usable)	(AY, GU, MS & Crossbreds)
Y – Likely		
N – Unlikely		
U - Unable to test (no genotype / blank pedigree)		
I – Dam Incorrect		
H - Unlikely; MGS suggestion based on haplotype tes	t	
S - Unlikely; Dam's sire is wrong based on haplotype	test	
X - Unlikely; No MGS suggestion		

Animal ID	Sample ID	Chip Type	Sire ID	Sire Status Code	Suggested Sire	Dam ID	Dam Status Code	Suggested Dam	MGS Status Code	MGS Sugg1-4	MGS Stat1-4	Usability Indicator	Parentage Indicator	Date
HOUSAF0001 23456789	HAU01234 56A-01	50K	HOUSAM0001 23456789	Y,N,U	HOUSAM0009 87654321	HOUSAF0001 23456789	Y,N,U	HOUSAF0009 87654321	Y,N,U,I,H,S,X	HOUSAM0 001234567 89	3	Y,N,L,M,U	N,P,R,B	20111018

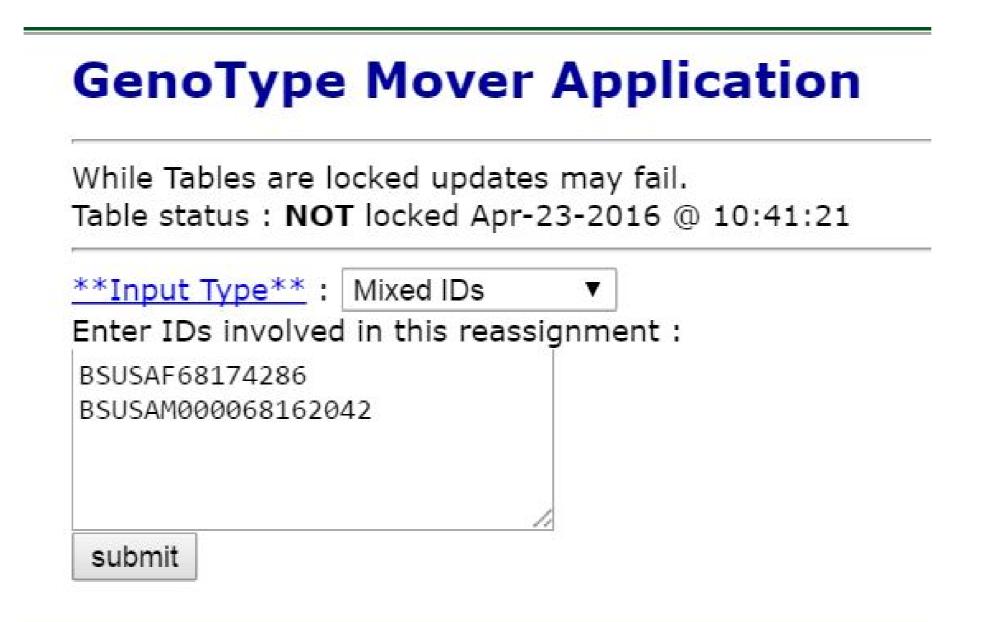


MGS STAT

H,S - Expected value 45.0;

Genotype Move/Swap APP

- This application is used when a genotype has to be re-assigned to another animal
- You can indicate if the ID that is entered in the box is Animal ID or sample ID by choosing Input Type (Mixed IDs, Animal IDs only, or sample IDs only)
- "S+" in front of ID means that the ID that is following S+ is a sample ID, not an animal ID





How to Assign a genotype to a different animal (includes providing missing assignments)

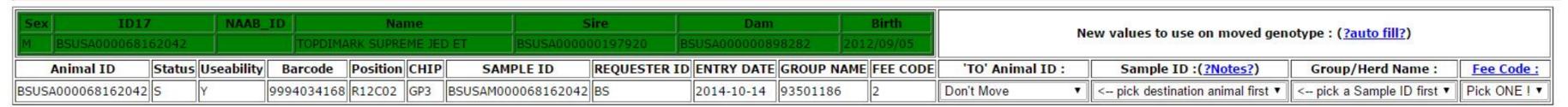
- You MUST include all sources and destination animals (or sample IDs) in the query form.
- If a genotype has NOT been assigned to an animal you must use 'Sample IDs only' or 'Mixed IDs' in the query form to list that genotype.



input:BSUSAF68174286



input:BSUSAM000068162042





getfee

This application searches fee code, based on given "ANIMAL ID"

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6. Nomination and Data Correction through FTP



What is difference between fmt1 record submission through FTP and WebQuery?

comparison	FTP	Web Query
Easiness	have to follow fmt1 format	easy to submit record (no need to worry about format)
Amount of records/ submission	allows batch submission	one by one submission
Record Type flexibility	multiple record type accepted (P,X,C,R etc)	Pedigree (P) only
System	automated system can be developed by the requester	manual work involved

Summary:

Web Query is easy to use and need to use it to accomplish some tasks, however, it might worth investing some time and effort to build your own system to submit format through FTP, as it is flexible and efficient, sometimes.



Format1 Error file (notify file) YYYYMMDD.1EX/notify.YYYYMMDD.1(G)X

0FH0AIP1111111111111H0AIP222222222222

HOAIP33333333333320110913A20151119R211000000001706653



- Once you submit format1 in "IN" directory and the data is processed, you may receive format1 error file, if there is any
 errors
- The error file looks similar to format1, but has extra data describing error information (in green box).
- The codes in red box tell you what kind of errors the submitted format1 has.
- https://www.uscdcb.com/formats/geterr.cfm has all possible errors and description of the errors
- Resubmit corrected record.

4Jn	Input sire identification and master file sire identification for animal (@3-19) are not the same. Cross-reference ignored.	Change	Notify – submission accepted, but something needs to be aware Change-submission accepted, but the reflected change
oGg	Animal identification (@3-19) cannot be re- tagged identification (@54-70) for record type code of 'R'.	Reject	might be bit different from what you submitted Reject – rejected because something in your record was wrong



Summary

- List of things to do as a nominator
 - Communicate with your customer to arrange sample collection
 - Communicate with the lab to coordinate the schedule
 - Nominate animals before the genotypes are sent to CDCB
 - Check if pedigree and nomination were successfully loaded to CDCB database by checking format1E/notify file
 - Correct errors from pedigree and nomination submission
 - Once genotypes are loaded by the lab, check existence of genomic conflicts
 - Resolve the genomic conflicts, in order to make the genotype usable
 - You should expect weekly evaluation results (if the genotype was new) and monthly evaluations if everything is correct. So check the evaluation schedule
 - Distribute the evaluation results to your customers once you receive evaluation results from us
 - More detailed documentations available on Redmine
 - Ezequiel will discuss on it later
 - > Do not hesitate to contact me if you have any questions or requests



Thank you and any questions??

