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Uniformity of Rotavirus Strain Nomenclature Proposed by the Rotavirus Classification Working Group (RCWG)

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Abstract

In April 2008, a nucleotide sequence-based, complete genome classification system was developed for group A rotaviruses (RVs). This system assigns a specific genotype to each of the 11 genome segments of a particular RV strain according to established nucleotide percent cut-off values. Using this approach, the genome of individual RV strains are given the complete descriptor of Gx-P[x]-Ix-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx. A Rotavirus Classification Working Group (RCWG) was formed by scientists in the field to maintain, evaluate, and develop the RV genotype classification system, in particular to aid in the designation of new genotypes. Since its conception, the group has ratified 50 new genotypes: as of January 2011, new genotypes for VP7 (G20–G26), VP4 (P[28]–P[35]), VP6 (I12–I16), VP1 (R5–R9), VP2 (C6–C9), VP3 (M7–M8), NSP1 (A15-A16), NSP2 (N6-N9), NSP3 (T8-T12), NSP4 (E12-E14), and NSP5/6 (H7-H11) have been defined for RV strains identified in humans, cows, pigs, horses, mice, South American camelids (guanaco and vicuña), chickens, turkeys, pheasants, and bats. With increasing numbers of complete RV genome sequences becoming available, a standardized RV strain nomenclature system is needed and the RCWG proposes that individual RV strains are named as follows: RV group/species of origin/country of identification/common name/year of identification/G- and Ptype. In collaboration with the National Center for Biotechnology Information (NCBI), the RCWG is also working on developing a RV-specific resource for the deposition of nucleotide sequences. This resource will provide useful information regarding RV strains, including but not limited to, the individual gene genotypes, epidemiological, and clinical information. Together, the proposed nomenclature system and the NCBI RV resource will offer highly useful tools for investigators to search for, retrieve, and analyze the ever-growing volume of RV genomic data.

Keywords

Rotavirus; Classification; Nomenclature; Strain; Nomenclature guidelines

Introduction

Rotaviruses (RVs) are members of the *Reoviridae* family and cause severe diarrheal illness in the young of various animal species (24). In humans, RV infections lead to the death of more than 500,000 infants and young children each year, particularly in developing regions of the world (69). RVs possess a genome consisting of 11 segments of double-stranded (ds) RNA (24). Most segments encode a single polypeptide, allowing the virus to express six structural viral proteins (VPs) and five non-structural proteins (NSPs) (24). However, in some group A RV strains, a second open-reading frame (ORF) is detected in genome

segment 11, leading to the expression of another protein product (NSP6) (33) in addition to NSP5. The viral particle has icosahedral symmetry and is composed of three concentric protein layers (24, 62). VP7 and VP4 are the components of the outermost protein layer (outer capsid), and each carries neutralizing epitopes (24). The middle protein layer (inner capsid) is composed of VP6 and surrounds the inner layer (the core shell) which is composed of VP2 (62). Comprised within the core shell are the viral RNA-dependent RNA polymerase (VP1) and RNA capping enzyme (VP3), as well as the 11 dsRNA genome segments (24). The RV NSPs have various functions in the replication and morphogenesis of RV progeny and in evasion of the host immune response (24). Based on the antigenic properties of VP6, RVs have been subdivided into 5 serological species (A–E) and two additional tentative species (F and G) according to the International Committee on Taxonomy of Viruses (ICTV) (3, 75). These "RV species" are commonly referred to as "RV groups". RVs belonging to species A, B and C (RVA, RVB and RVC, respectively) are known to infect humans and various animals, whereas RVs of species D, E, F and G (RVD, RVE, RVF and RVG, respectively) thus far have only been identified in animals, mostly birds (3, 54). Epidemiologically, RVA is the most important for human infection and disease and have been classified further using various approaches. Specifically, RVA have been categorized based on the: (i) antigenic properties of VP6, VP7, and VP4 (subgroups, Gserotypes, and P-serotypes, respectively); (ii) migration pattern of the RNA genome segments when subjected to polyacrylamide gel electrophoresis (long, short, supershort or atypical electropherotypes); (iii) Whole genome RNA hybridization patterns (genogroups); and (iv) nucleotide sequence analyses (genotypes) (24, 50). Due to the segmented nature of the RV genome, reassortment events can occur after co-infection between RV strains belonging to the same group/species both in vitro and in vivo (26, 32, 61). Numerous examples of such gene exchanges are available in literature for RVA strains (46, 54). Recent data also suggests that reassortment involving the NSP1-encoding genome segment may have occurred between ancestral strains of avian RVA and RVD (87). However, there is no evidence for reassortment among contemporary RVs that belong to different groups/species. Their inability to undergo segment exchange, even under experimental conditions, indicates that RV groups can be thought of as unique viral species (3).

In April 2008, a nucleotide sequence-based, complete genome classification system was developed for RVA strains (51). This system assigns a specific genotype to each of the 11 RV genome segments according to established nucleotide percent cut-off values. The VP7-VP4-VP6-VP1-VP2-VP3-NSP1-NSP2-NSP3-NSP4-NSP5/6 genes of RV strains are described using the abbreviations Gx-P[x]-Ix-Rx-Cx-Mx-Ax-Nx-Tx-Ex-Hx (x = Arabic numbers starting from 1), respectively (51). Full genome analyses have increased our recognition of the relatedness between animal and human RV strains, and highlights the relevance of a common nomenclature for both animal and public health. To maintain, evaluate, and develop this system, a Rotavirus Classification Working Group (RCWG) was formed (52), which includes researchers worldwide.

In this article, we report on the current status of genotype diversity for RVA strain that has been identified to date by the RCWG. Moreover, the RCWG is also working with researchers at the National Center for Biotechnology Information (NCBI) to develop a specific database for the deposition of RV sequence information. This RV resource will contain complete genome sequences that are annotated using VIGOR (VIral Genome ORF Reader) (94), as well as multiple types of metadata (epidemiological, clinical, etc.) to provide useful additional information to investigators. The new RV database will be very similar to the "Influenza Virus Resource" which is widely used to monitor influenza strains (9). As part of the database development, the RCWG herein proposes a standardized nomenclature for RV strains, which is similar to that already established for influenza

viruses. Universal adoption of this new system by the RV community will be crucial for the retrieval of relevant information from the RV resource.

Update from the RCWG

The task of the RCWG is to maintain, evaluate, and develop the RV genotype classification system. When the nucleotide sequence from a RVA strain of a potential new genotype is submitted to the RCWG, a thorough phylogenetic analysis is performed, and this analysis is reviewed by the members of the RCWG. When a consensus is reached, the submitter receives an e-mail with the novel genotype number(s) of the particular gene(s), which can then be used in publications. To facilitate the utilization of the RV genotype classification system, a regularly updated online automatic web application, RotaC (http://rotac.regatools.be/), was developed (45).

Since the establishment of the RCWG, its activities have been reviewed at annual face-to-face meetings, held in conjunction with major scientific virology meetings. The first 3 RCWG-meetings were held at: (i) the 27th annual meeting of the American Society for Virology (ASV) (July 14th, 2008, Ithaca, New York), (ii) the 10th International Symposium on dsRNA Viruses (July 24th, 2009, Hamilton Island, Australia), and (iii) the 29th annual meeting of the ASV (July 19th, 2010, Bozeman, Montana). The fourth and fifth RCWG meetings are planned to take place during the 30th annual meeting of the ASV in Minneapolis, Minnesota (July 16 th –20 th, 2011) and the 11th International Symposium on dsRNA Viruses in San Juan, Puerto Rico (November 27 th –December 1 st, 2012), respectively.

Table 1 contains a list of RV strains possessing new genotypes that have been recognised by the RCWG since the introduction of the classification system in April 2008. The new genotypes were found in RVs identified in a variety of host species including humans, cows, pigs, horses, mice, chickens, turkeys, pheasants, South American camelids, and bats. Several of these new genotypes have been published (1, 18, 23, 30, 42, 55, 56, 81, 83, 86, 90). For several other strains, such as RVA/Human-tc/ITA/260-97/1997/G3P[3] (HQ661112-HQ661122), RVA/Cow-tc/JPN/Dai-10/2007/G24P[33] (AB513836-AB513837 and AB573070-AB573078), RVA/Mouse-tc/USA/ETD_822/XXXX/G16P[16] (GQ479947-GQ479957), RVA/Pig-wt/JPN/FGP51/2009/G4P[34] (AB571046-AB571047), and RVA/Pig-wt/JPN/TJ4-1/2010/G26P[unknown] (AB605258), at present only the GenBank accession numbers are available. Table 2 shows RV strains of all recognised genotypes that are not represented in Table 1.

Although the RV classification system has so far been limited to that of RVA strains, the RCWG plans to develop similar systems for RV strains belonging to other RV groups/ species once a critical number of complete genome sequences become available. The complete genomes of 4 human RVB strains were recently sequenced and analyzed by Yamamoto and colleagues, bringing the total number of genomes to 8 (7 human RVB strains and a single murine RVB strain) (67, 98). So far, all of the fully analyzed human RVB strains were detected in China and South-East Asia (Bangladesh, India, and Myanmar). Regarding RVC strains, the entire genome sequences have been determined for only 8 strains: the porcine strain Cowden and 7 human strains detected in the UK, Japan, China, Bangladesh and India (11, 14, 99). The first complete genome sequence of a RVD strain (RVD/chicken-wt/DEU/05V0049/2005/GXP[X]), was published recently (87). Furthermore, the complete genome sequences of two Novel Adult Diarrhea Rotavirus (NADRV) strains (RVX/Human-tc/CHN/NADRV-J19/1997/GXP[X], and RVX/Human-wt/BAN/NADRV-B219/2002/GXP[X]), causing diarrhea in adults, have been determined (37, 67, 100). These NADRV strains have not yet been assigned to a RV group/species by ICTV. Recently, VP6

sequence information was obtained for avian RVF and RVG strains (38). In the future, analysis of these sequence data should allow the calculation of sequence-based thresholds to define (new) RV groups/species and genotypes within groups/species. A detailed overview of the current classification for non-RVA strains was recently published (54).

Proposed nomenclature of RV strains

Currently, no guidelines exist for the naming of RV strains. The lack of a standardized nomenclature system has lead to discrepancies in the literature where researchers have developed their own naming systems. With increasing numbers of complete RV genome sequences becoming available, and with the development of specific resources to retrieve and analyze these sequences, a more uniform nomenclature is clearly needed. The RCWG has discussed this issue, and we propose the following nomenclature for individual strains:

RV group/species of origin/country of identification/common name/year of identification/G-and P-type

A) Guidelines for wild type RV strains

These guidelines apply to any wild type RV strain or naturally occurring reassortant RV strain recovered from human or animal populations, which have been sequenced directly from clinical specimens (such as stool, blood or tissue samples), or environmental samples. Guidelines for nomenclature of: i) tissue culture-adapted RV strains, ii) RV vaccine strains, iii) RV strains that have been generated in the laboratory by reassortment, or iv) RV strains engineered in the laboratory by reverse genetics or equivalent mechanisms are provided further below in sections B), C), D and E).

- RV group/species: RVA, RVB, RVC, RVD, RVE, RVF or RVG. RVX should be
 used in cases where a strain has not yet been assigned to an established or new RV
 group/species.
- Species of origin: The "species of origin" field contains two components. The first component is: human, pig, cow, dog, cat, rhesus, simian, horse, rabbit, mouse, goat, sheep, guanaco, bat, turkey, chicken, pheasant, or other as appropriate. In case the sample was obtained from the environment (i.e., sewage, soil, river, lake, ocean or similar), "Env" should be used. In case the species of origin is unknown, "X" should be used. The second component is "-wt" (for wild type) to distinguish from tissue culture-adapted (-tc) and laboratory-generated or -engineered (-lab) RV strains. If a tissue culture-adapted or laboratory-generated strain is introduced into the population (e.g., a vaccine strain), and later recovered from a human or animal, the species from which the sample was identified should be used followed by "-wt".
- Country of identification: using a unique 3-letter abbreviation code for each country according to:
 https://www.cia.gov/library/publications/the-world-factbook/appendix/appendix-d.html. In case the country of identification is unknown, "XXX" should be used. If a tissue culture-adapted or laboratory-generated RV strain is introduced into the population and later recovered from a human or animal, the country from which the sample was recovered should be used (Further details, e.g. of city/site of identification, can be added in the common name or the metadata, see below).
- *Common name*: Short name given by investigators, preferentially not using forward slashes ("/") or backslashes ("\") to avoid confusion and computer processing problems. If appropriate, the common name can contain geographically or

- clinically important information, as long as the number of characters is less than/equal to 15.
- Year of identification: using the "yyyy" format. In case the year of identification is unknown, "XXXX" should be used. If a tissue culture adapted or laboratory-generated strain is introduced into a population and later recovered from a human or animal, the year in which the sample was identified should be used.
- *G-type*: using the form Gx, where x is the established G genotype/serotype number. If the G-type is unknown GX should be used.
- *P-type*: using the form Py[z], where y is the established P *sero*type number and z [in square brackets] is the established P *geno*type number. If the P-serotype is unknown, P[z] should be used, and if the P-genotype is unknown Py[X] or P[X] should be used.

Examples of strain names using this nomenclature system can be found in Tables 1 and 2.

B) Guidelines for tissue culture-adapted RV strains or RV strain passaged in vivo in their homologous host species

These guidelines apply to any non-vaccine RV strain which has been tissue culture adapted, or passaged *in vivo* in a homologous animal model, without the intention to introduce specific changes in the genome sequence. Specific details about the number of passages and the used cell lines or animal should be provided in the metadata. Guidelines for nomenclature of: i) RV vaccine strains, ii) RV strains that have been generated in the laboratory by reassortment, or iii) RV strain engineered in the laboratory by reverse genetics or equivalent mechanisms are provided below in sections C), D) and E).

- *RV group/species*: See section A) above.
- Species of origin: The "species of origin" field contains two components. The first component is: human, pig, cow, dog, cat, rhesus, simian, horse, rabbit, mouse, goat, sheep, bat, guanaco, turkey, chicken, pheasant, or other as appropriate. In case the sample was obtained from the environment (i.e., sewage, soil, river, lake, ocean or similar), "Env" should be used. In case the species of origin is unknown, "X" should be used. The second component is "-tc" (for tissue cultured) or "-hhp" (homologous host passaged) to distinguish from wildtype (-wt) and laboratory generated or engineered (-lab) RV strains. If a tissue culture-adapted or in vivo passaged RV strain is introduced into the population (e.g., a vaccine strain), and later recovered from a human or animal, the species from which the sample was identified should be used followed by "-wt".
- Country of identification: using a unique 3-letter abbreviation code for each country according to: https://www.cia.gov/library/publications/the-world-factbook/appendix/appendix-d.html. In case the country of identification is unknown; "XXX" should be used. If a tissue culture-adapted RV strain is introduced into the population and later recovered from a human or animal, the country from which the sample was recovered should be used (Further details, e.g. of city/site of identification, can be added in the common name or the metadata, see below).
- *Common name*: See section A) above
- Year of identification: using the "yyyy" format. In case the year of identification is
 unknown, "XXXX" should be used. If a tissue cultured strain is introduced into a
 population and later recovered from a human or animal, the year in which the
 sample was identified should be used.

- *G-type*: See section A) above.
- *P-type*: See section A) above.

Examples of strain names using this nomenclature system can be found in Tables 1 and 2.

C) Guidelines for RV strains *generated in a laboratory* for which a host species can be assigned unambigously

These guidelines apply to any RV strain in which small deliberate changes have been introduced (examples: chemically mutagenised RV strain, moderately modified RV strain using reverse genetics techniques, etc.) or RV strains passaged in heterologous animal model, and for which there is no ambiguity about the original host species. Specific details about the introduced changes and the methods used should be provided in the metadata. Guidelines for nomenclature for: i) RV vaccine strains, ii) RV strains that have been generated in the laboratory by reassortment, iii) RV strains with a designed synthetic sequence generated using reverse genetics, or iv) RV strains in which large modifications have been applied using reverse genetics or equivalent mechanisms are provided below in sections D) and E).

- RV group/species: See section A) above.
- Species of origin: The "species of origin" field contains two components. The first component is: human, pig, cow, dog, cat, rhesus, simian, horse, rabbit, mouse, goat, sheep, bat, guanaco, turkey, chicken, pheasant, or other as appropriate. In case the sample was obtained from the environment (i.e., sewage, soil, river, lake, ocean or similar), "Env" should be used. In case the species of origin is unknown, "X" should be used. The second component is "-lab" (lab engineered) to distinguish from wildtype (-wt) and tissue culture (-tc) adapted RV strains. If a laboratory-generated strain is introduced into the population (e.g., a vaccine strain), and later recovered from a human or animal, the species from which the sample was identified should be used followed by "-wt".
- Country of identification: using a unique 3-letter abbreviation code for each country according to:
 https://www.cia.gov/library/publications/the-world-factbook/appendix/appendix-d.html. In case the country of identification is unknown; "XXX" should be used. If a laboratory-generated strain is introduced into the population and later recovered from a human or animal, the country from which the sample was recovered should be used (Further details, e.g. of city/site of identification, can be added in the common name or the metadata, see below).
- Common name: See section A) above.
- Year of identification: using the "yyyy" format. In case the year of identification is unknown, "XXXX" should be used. If a laboratory-engineered strain is introduced into a population and later recovered from a human or animal, the year in which the sample was identified should be used.
- *G-type*: See section A) above.
- *P-type*: See section A) above.

Examples of strain names using this nomenclature system can be found in Tables 2.

D) Guidelines for RV strains *generated in a laboratory* for which a host species cannot be assigned unambiguously

These guidelines for nomenclature apply to RV strains that have been generated in the laboratory by reassortment, strains with a designed synthetic sequence generated using reverse genetics, strains in which large modifications have been applied using reverse genetics or RV strains generated by combinations of the above procedures. Specific details about the introduced changes and the used methods should be provided in the metadata.

RV group/species: See section A) above.

Species of origin: "LabStr". More specific details about the procedure used to create the virus should be provided in the metadata.

- Country of identification: The country in which the RV strain was generated should be provided according to the unique 3-letter abbreviation code for each country: https://www.cia.gov/library/publications/the-world-factbook/appendix/appendix-d.html.
- Common name: Short name given by investigators, preferentially without the use of forward slashes ("/") or backslashes ("\") to avoid confusion. If appropriate, the common name can contain specific information about the laboratory strain, such as the procedure used to generate it, as long as the number of characters is less than or equal to 15.
- *Year of identification*: The year in which the RV strain was generated should be provided using the "yyyy" format.
- *G-type*: See section A) above.
- *P-type*: See section A) above.

Examples using this nomenclature system for naming laboratory strains can be found in Table 3.

E) Guidelines for RV vaccine strains

Due to the increasing use of live-attenuated RV vaccine, it will be important to distinguish vaccine strains from naturally-occurring wild type strains. Therefore, a specific notation for vaccine strains was developed and should be used if the strain is the sole component or part of a multi-component live vaccine.

RV group/species: See section A) above.

- *Species of origin*: "Vaccine". Further specific details about the generation of the vaccine strain should be provided in the metadata.
- Country of identification: The country in which the vaccine was identified (in case
 of a vaccine containing a tissue culture adapted strain) or developed (in case of a
 vaccine developed using reassortment or in vitro engineering) should be provided
 according to the unique 3-letter abbreviation code for each country:
 https://www.cia.gov/library/publications/the-world-factbook/appendix/appendixd.html.
- *Common name*: Short name given by investigators, preferentially without the use of forward slashes ("/") or backslashes ("\") to avoid confusion. It is recommended that the commercial name of the vaccine is included in the common name. The number of characters should be less or equal than 15.

Year of identification: The year in which the RV strain was identified (in case of a
vaccine containing a tissue culture adapted strain) or developed (in case of a
vaccine developed using reassortment or in vitro engineering) should be provided
using the "yyyy" format.

- *G-type*: See section A) above.
- *P-type*: See section A) above.

Examples using this nomenclature system for naming vaccine strains can be found in Table 3

RV resource under development at NCBI

Due to the rapid increase in the number of complete RV genome sequences available, the RCWG is working with NCBI to develop an advanced RV resource, which will include a value added database and a suite of tools for the analysis of RV sequences. When new sequence records are submitted to GenBank their contents will be added to the RV database through an automated process. A web based interface will allow researchers to search the RV database using a variety of genetic, epidemiological and clinical criteria, retrieve relevant sequences, and analyze them. With this in mind, the RCWG proposes that the following list of biological descriptors (if available and relevant) should be included with sequence records submitted to GenBank. This list of metadata was agreed upon by members of the RCWG, but is by no means exclusive, as additional metadata can also be added.

Strain specific features

- **a.** Wild type primary strain
 - **b.** Cell culture-adapted strain
 - c. In vitro-generated reassortant strain
 - **d.** Strain engineered by reverse genetics procedures
 - **e.** *In vitro*-generated reassortant RV strain or RV strain engineered by reverse genetics, which was identified in nature from any host (e.g., a vaccine strain identified in a human infant)
 - **f.** *In vivo*-generated strain resulting from reassortment of a laboratory-generated strain and a wild type strain (e.g., a strain recovered from a vaccinated infant that is the result of a reassortment event of the vaccine stain and a wild type strain)
- In cases b, c, and d, more details should be provided to account for any engineered changes. It is important to note that natural reassortant RVs should be categorized as "wild type strains", as long as none of the "parents" of the reassorted strains belong to categories b, c, or d
- Genotypes of remaining 9 RNA segments according to RCWG guidelines (52)
- Species/group (RVA, RVB, RVC, RVD, RVE, RV F, RVG, or RVX)
- For RVA: subgroup (SG, I, II, I+II, non-I/non-II) specificity
- Electropherotype: long, short, super-short, or atypical
- Banding pattern (example: 4:2:3:2 for RVA, 4:2:2:3 for RVB, 4:3:2:2 for RVC, etc.)
- Region of identification: country, state, province, city/village

 Latitude/longitude (LAT/LON) coordinates: a Google Earth-like application might be incorporated where the location can be pinpointed on a map, and the coordinates will be added automatically

• Collection date: time of sample collection (year, month, and day)

Host specific features

- Host species: both the "common english name" as the scientific Latin name
- Host date of birth
- Host age at infection (or date of sample collection)
- Host gender
- Vaccination status of host
- Name of administered vaccine, number of administered doses and vaccination dates
- For animal RV vaccines: adjuvant used (oil or aqueous) and RV genotypes and/or other microbes included in the vaccine

Disease related and clinical features

- Symptomatic or asymptomatic infection
- Clinical symptoms of host: diarrhea, vomiting, fever, other
- Clinical severity: mild, moderate, severe using established clinical gastroenteritis severity scoring systems (Vesikari, Clark, other) (16, 27, 79, 80) or World Health Organization (WHO) ref schemes
- Clinical outcome: dehydration (using WHO or Gorelick ref schemes) (34, 96), emergency room or its equivalent (outpatient), hospitalization and/or death
- Sample type: Stool, serum, nasal swabs, or other systemic tissues (lung, brain, etc)
- Other co-infecting agents detected
- For RVs detected in domestic animals (calves, foals, piglets, etc): indicate if the
 animal received electrolytes solutions, antibiotic, anti-diarrheic or other unspecific
 treatment before and/or after sample collection
- Sample derive from a single case of diarrhea or an outbreak. In case of an outbreak, what were the morbidity and mortality rates
- For animals indicate type of exploitation (dairy or beef herds; extensive or intensive production; thorough-bred or standard-bred horses, etc)

Analyses specific information

- Was sequencing performed on stool, rectal swab, intestinal content, other type of sample of the patient, environmental sample or on cell culture-adapted virus?
- Cell type (e.g. Vero) and number of times the virus was passaged in cell culture before sequencing
- Sequencing method: Sanger sequencing, pyrosequencing, other
- Termini: Were the 5' and 3' terminal sequences primer-derived or sequenced de novo?

Conclusions

The quickly evolving sequencing capabilities of research laboratories and commercial organizations around the world have resulted in a rapid growth of sequence data for RVs, and dealing with these data has become a major challenge. In an attempt to introduce a systematic method of naming RV strains, the RCWG proposes the following nomenclature: RV group/species of origin/country of identification/common name/year of identification/G and P-type. In this nomenclature, specific guidelines were developed for wild type RV strains, tissue culture adapted strain, RV vaccine strains, as well as RV strains that have been generated or engineered in a laboratory using reassortment or reverse genetics procedures. This standardized naming procedure is reminiscent of the nomenclature guidelines for influenza viruses and will be very useful for future analyses. However, this system will only succeed if the entire research community supports and adheres to the proposed guidelines. It should be noted that the terms "RV groups" and "RV species" are used interchangeably.

Towards utilizing the large amount of RV nucleotide sequence data, a RV specific database is being developed by the NCBI, which is expected to be launched in the second half of 2011. This resource will be similar to the NCBI Virus Variation resources developed for influenza and dengue viruses (9, 77) and the resources developed at the Los Alamos National Laboratory for hepatitis C virus (HCV) (41) and for human immunodeficiency virus (HIV) (www.hiv.lanl.gov./content/). RV nucleotide sequence data, as well as metadata describing the biological and epidemiological context of associated sequences, will be stored in specially designed relational databases. A new, user-friendly web interface will allow investigators to construct and explore resource queries based on a variety of criteria. Additionally, novel web-based tools and displays will allow users to compare retrieved nucleotide and protein sequences on the basis of chronology, geography, and biological significance. In order to fully exploit the possibilities of such a resource for the study of viral epidemiology, seasonality, geographical spread, links between specific strains and clinical manifestations, possible vaccine escape-mutants, etc., it is imperative that nucleotide sequence submissions include relevant metadata. In addition, the RCWG strongly encourages researchers to retrospectively update the names of their RV sequences in GenBank, and add relevant metadata to the files. This process is straightforward and will greatly enhance the scientific potential of individual sequence records. From Table 1 it is obvious that close monitoring, updating and genotype assignment activities of the RCWG as practiced during the past 3 years are absolutely necessary to sustain and develop the new RV genotype-based classification and nomenclature system. With the increasing number of sequence data becoming available for non-RVA strains, the activities of the RCWG will probably be expanded in the near future.

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Table 1

RV strains possessing novel genotypes assigned by the RCWG since its formation in April 2008 (51, 52). Strain name, available genotype constellation and publication are shown. Novel assigned genotypes are in bold.

CUTD ATM MANATE					NEV	V GEN	NEW GENOTYPES					110
STRAIN NAME	VP7	VP4	AP6	VP1	VP2	VP3	NSP1	NSP2	£dSN	NSP4	NSP5	KEF.
RVA/Human-wt/ECU/Ecu534/2006/G20P[28]	G20	P[28]	113									(83)
RVA/Cow-wt/JPN/Azuk-1/2006/G21P[29]	G21	P[29]	71	R2	C2	M2	A13	N2	6L	E2	НЗ	(1)
RVA/Guanaco-wVARG/ChubuV1999/G8P[14]	RS	P[14]	12	R5	C2	M2	A3	N2	9L	E12	НЗ	(55)
RVA/Chicken-tc/DEU/02V0002G3/2002/G19P[30]	G19	P[30]	111	R6	9 .	M7	A16	9N	8L	E10	8Н	(98)
RVA/Turkey-tc/DEU/03V0002E10/2003/G22P[35]	G22	P[35]	14								H4	(81), N.P.
RVA/Chicken-tc/DEU/06V0661/2006/G19P[31]	G19	P[31]	I11								8H	(81)
RVA/Human-wt/NPL/KTM368/2004/G11P[25]	G11	P[25]	112	R1	Cl	M1	A1	N1	$_{ m LI}$	E1	H1	(56)
RVA/Human-tc/ITA/260-97/1997/G3P[3]	G3	P[3]	13	R3	C3	M3	A15	N2	£L	E3	9H	N.P.
RVA/Horse-wt/ARG/E30/1993/G3P[12]	G3	P[12]	9I	R2	C2	M3	A10	N2	£L	E2	Н7	N.P.
RVA/Pig-wt/IRL/61/07-ire/2007/G2P[32]	G2	P[32]	IS							6 3		(18)
RVA/Pheasant-wVHUN/Phea14246/2008/G23P[?]	G23											(06)
RVA/Pig-wt/CAN/CE-M-06-0003/2005/G2P[27]	G2	P[27]	114									(42)
RVA/Cow-tc/JPN/Dai-10/2007/G24P[33]	G24	P[33]	12	R2	C2	M2	A13	N2	6L	E2	Н3	(1)
RVA/Mouse-tc/USA/ETD_822/XXXX/G16P[16]	G16	P[16]	17	R7	C7	M8	A7	N7	01L	E7	6Н	N.P.
RVA/Bat-wt/KEN/KE4852/07/2007/G25P[6]	G25	P[6]	115	RY^a	C8			8N	III	E2	H10	(23)
RVA/Pig-wt/JPN/FGP51/2009/G4P[34]	G4	P[34]										N.P.
RVA/Human-tc/KEN/B10/1987/G3P[2]	G3	P[2]	116	R8	CS	M5	A5	N5	L2	E13	H5	(30)
RVA/Pig-wt/JPN/TJ4-1/2010/G26P[?]	G26											N.P.
RVA/Horse-tc/GBR/L338/1991/G13P[18]	G13	P[18]	9I	R9	C3	M6	A6	N9	T12	E14	H11	N.P.

and sequences of this gene segment have been determined, but it could not be assigned to any of the established genotypes. It may be the representatives of a new genotype, but the entire ORF needs to be determined as stated in the guidelines from the RCWG (52), before this can be confirmed.

An open space refers to: genotype not known, as sequencing has not been performed.

Abbreviation: N.P., not published.

Table 2

List of RV strains representing all the currently established genotypes except for those represented in Table 1.

Matthijnssens et al.

LL R T A LAR T GALLO						GENOTYPES	YPES					
DIRALIA NAIME	Λ	VP4	AP6	VP1	VP2	VP3	NSP1	ZdSN	8 NSP3	NSP4	NSP5	
RVA/Human-tc/USA/Wa/1974/G1P1A[8]	G1	P[8]	11	R1	Cl	M1	A1	N	T1	E1	H1	(51)
RVA/Human-wt/BGD/Dhaka16-03/2003/G1P[8]	G1	P[8]	11	R1	Cl	M1	A1	N	T1	E1	H1	(72)
RVA/Human-wt/USA/LB2719/2006/G1P[8]	G1	P[8]	11	R1	C1	M1	A1	IN	T1	E1	H1	(7)
RVA/Human-wt/IND/NIV929893/1992/G1P[19]	G1	P[19]	11							E1		(15)
RVA/Pig-wt/SVN/P21-5/2004/GIP[27]	G1	P[27]								E9		(84)
RVA/Human-tc/USA/DS-1/1976/G2P1B[4]	G2	P[4]	12	R2	C2	M2	A2	NZ	T2	E2	Н2	(51)
RVA/Human-wt/CHN/TB-Chen/1996/G2P[4]	G2	P[4]	12	R2	C2	M2	A2	NZ	T2	E2	Н2	(12)
RVA/Human-wt/USA/LB2744/2006/G2P[4]	G2	P[4]	12	R2	C2	M2	A2	NZ	T2	E2	Н2	(7)
RVA/Pig-wt/ESP/34461-4/2003/G2P[23]	G2	P[23]	15							E1	H1	(39)
RVA/Pig-wt/THA/CMP034/2000/G2P[27]	G2	P[27]	15							E9	H1	(39)
RVA/Simian-tc/ZAF/SA11-H96/1958/G3P5B[2]	G3	P[2]	12	R2	CS	M5	A5	SN.	TS	E2	H5	(82)
RVA/Simian-tc/USA/RRV/1975/G3P[3]	G3	P[3]	12	R2	C3	M3	49	NZ	T3	E3	9H	(09)
RVA/Human/USA/HCR3A/1984/G3P[3]	G3	P[3]	13	R3	C2	M3	6Y	N2	T3	E3	9Н	(88)
RVA/Cat-tc/AUS/Cat97/1984/G3P[3]	G3	P[3]	13	R3	C2	M3	6Y	N2	T3	E3	9Н	(88)
RVA/Dog-tc/USA/CU-1/1982/G3P[3]	C3	P[3]	13	R3	C2	M3	6Y	N2	£1	E3	9H	(88)
RVA/Human-wt/THA/CMH222/2001/G3P[3]	G3	P[3]	81							E3		(40)
RVA/Human-tc/AUS/RV3/1977/G3P2A[6]	G3	P[6]	11	R1	C1	M1	A1	IN	T1	E1	H1	(28)
RVA/Cow-lab/GBR/PP-1/1976/G3P[7]	C3	P[7]					A3			E8		(21)
RVA/Pig-tc/VEN/A131/1988/G3P9[7]	G3	P[7]	15	R1	C2	M1	A1	IN	T1	E1	H1	(51)
RVA/Human-tc/USA/P/1974/G3P1A[8]	G3	P[8]	11	R1	C1	M1	A1	N1	T1	E1	H1	(51)
RVA/Human-wt/USA/DC5544-Bethesda/1991/G3P[8]	C3	P[8]	11	R1	C1	M1	A1	IN	11	E1	H1	(63)
RVA/Cat-wt/ITA/BA222/2005/G3P[9]	G3	P[9]	12	R2	C2	M2	A3	IN	T3	E2	Н3	(49)
RVA/Human-tc/ITA/PAH136/1996/G3P[9]	C3	P[9]	12	R2	C2	M2	A3	IN	9L	E2	Н3	(19)
RVA/Human-tc?/ITA/PAI58/1996/G3P[9]	G3	P[9]	12	R2	C2	M2	A3	NZ	9L	E2	Н3	(19)
RVA/Cat-tc/AUS/Cat2/1984/G3P[9]	G3	P[9]	13	R3	C2	M3	A3	N1	9L	E3	Н3	(88)
RVA/Human-tc/JPN/AU-1/1982/G3P3[9]	G3	P[9]	13	R3	C3	M3	A3	N3	Т3	E3	Н3	(51)

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Ę	KEF.	(57)	(57)	(48)	(09)	(99)	(99)	(51)	(99)	(95)	(56)	(51)	(43)	(47)	(51)	(17)	(28)	(51)	(20)	(58)	(65)	(55)	(55)	(9)	(65)	(55)	(09)	(5)	(29)	
	NSP5	Н3	Н3		9H	H1	H1	H1	H1	H1	H1	H1			Н3	Н3	Н3	Н3	Н3	H2	H1	Н3	Н3	Н3		Н3	Н3	Н3	Н3	
	NSP4	E5	E5	E5	E3	E1	E1	E1	E1	E1	E1	E1	E1	E1	E2	E2	E2	E2	E2	E2	E1	E2	E2	E2	E11	E12	E2	E2	E2	
	NSP3	1E	T6		Т3	T1	T1	T1	T1	T7	T1	T1			T6	T6	1L6	T6	T7	T2		T6	T6	T6		T6	T6	76 C	T6	
	NSP2	N2	N2		N	N1	ΙΝ	Ξ	Ξ	Ξ	ΙΝ	N			N2	N2	N2	N2	N2	N2		N2	N2	N2		N2	N2	N2	N2	
YPES	NSP1	49	49		49	A8	A8	A1	A8	A1	A1	A1			A3	A3	A11	A3	A3	A2		А3	A11	A11		A13	А3	A13	A3	
GENOTYPES	VP3	M3	M3		M3	M2	M1	M1	M1	M1	M1	M1			M2	M2	M2	M2	M2	M2	M1	M2	M2	M2		M2	M2	M2	M	
	VP2	C2	C2		C3	C1	C1	CI	CI	CI	C1	C1			C2	C2	C2	C2	C2	C2	C1	C2	C2	C2		C2	C2	C2	C2	
	VP1	R2	R2		R3	R1	R1	R1	R1	R1	R1	R1			R2	R2	R2	R2	R2	R2	R1	R2	R2	R2		R5	R2	R2	R2	
	VP6	12	12		61	П	Π	Ξ	Ξ	IS	IS	П		IS	12	12	12	12	12	12	12	12	12	12	14	12	12	12	12	
	VP4	P[14]	P[14]	P[22]	P[24]	P[4]	P[6]	[6]	[6]	[6]	P[7]	[8]	P[23]	P[26]	P[1]	P[1]	P[1]	P[5]	P[5]	[9]d	P[13]	P[14]	P[14]	P[14]	P[17]	P[1]	P[1]	P[1]	P[1]	
	VP7	G3	G3	G3	G3	G4	G4	G4	G4	G4	G5	G5	G5	G5	9D	9D	G6	9D	9D	9D	9D	G6	9D	95	G7	C8	G8	85	G8	
COTTO A TAY NA A MATE	SIKALIN NAME	RVA/Human-wt/BEL/B4106/2000/G3P[14]	RVA/Rabbit-tc/ITA/30/96/1996/G3P[14]	${\rm RVA/Rabbit-wv/ITA/229/01/2001/G3P[22]}^a$	RVA/Rhesus-tc/USA/TUCH/2002/G3P[24]	RVA/Human-wt/IND/mani-253/2007/G4P[4]	RVA/Human-wt/IND/mani-362/2007/G4P[6]	RVA/Human-tc/GBR/ST3/1975/G4P2A[6]	RVA/Pig-tc/USA/Gottfried/1983/G4P[6]	RVA/Human-tc/CHN/R479/2004/G4P[6]	RVA/Pig-tc/USA/OSU/1977/G5P9[7]	RVA/Human-tc/BRA/IAL28/1992/G5P[8]	RVA/Pig-tc/VEN/A34/1985/G5P[23]	RVA/Pig-wt/ITA/134/04-15/2003/G5P[26]	RVA/Cow-tc/VEN/BRV033/1990/G6P6[1]	RVA/Cow-tc/FRA/RF/1982/G6P[1]	RVA/Goat-tc/BGD/GO34/1999/G6P[1]	RVA/Cow-tc/USA/WC3/1981/G6P[5]	RVA/Cow-tc/GBR/UK/1973/G6P7[5]	RVA/Human-wt/BEL/B1711/2002/G6P[6]	RVA/Human-wt/IND/HP140/1987/G6P[13]	RVA/Human-wt/BEL/B10925-97/1997/G6P[14]	RVA/Human-wt/HUN/Hun5/1997/G6P[14]	RVA/Human-wt/HUN/BP1879/2003/G6P[14]	RVA/Turkey-tc/IRL/Ty-3/1979/G7P[17]	RVA/Guanaco-wt/ARG/Rio_Negro/1998/G8P[1]	RVA/Rhesus-tc/USA/PTRV/1990/G8P[1]	RVA/Human-wt/NIC/NIC522/2008/G8P[1]	RVA/Human-tc/KEN/B12/1987/G8P[1]	

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4	KEF.	(89)	(02)	(65)	(65)	(51)	(8)	(55)	(51)	(51)	(64)	(64)	(78)	(91)	(99)	(99)	(22)	(22)	(74)	(26)	(13)	(4)	(99)	(51)	(99)	(99)	(73)	(73)	(73)
	NSP5		H2	H2	H2	H2	Н3	Н3	H1	H1	H1	H1	H1	H1	H1	H2	H1	H1	Н3	Н3	Н3	H1	H1	H1	H1	H1	H1	H1	H1
	NSP4		E2	E2	E2	E2	E2	E2	E1	E1	E1	E1	E1	E1	E1	E2	E1	E1	E2	E2	E2	E1	E1	E1	E1	E1	E2	E1	E1
	NSP3		T2	T2	T2	T2	7F	T6	T1	T1	T1	T1	T1	T1	T1	T2	T1	T1	T1	T6	1E	T1	T1	T1	T1	T1	T2	T1	T2
	NSP2		N2	N2	N2	N2	N2	N2	Z	Z	N1	Z	Z	Z	NI	N2	NI	NI	NI	N2	N2	NI	NI	NI	NI	Z	N	Z	ΙΝ
YPES	NSP1	A14	A2	A2	A2	A2	A11	A11	A1	A1	A1	A1	A1	A1	48	A3	A1	A1	A1	A3	A11	A1	48	A1	A1	A1	A2	A1	A1
GENOTYPES	VP3		M2	M2	M2	M2	M2	M2	M1	M1	M1	M1	M1	M1	M1	M2	M1	M1	M2	M2	M2	M1	M1	M1	M1	M1	M1	M1	M1
	VP2		C2	C2	C2	C2	C2	C2	CI	CI	C1	C1	C1	CI	C1	C2	C1	C1	C2	C2	C2	C1	C1	C2	C1	C1	C2	C1	Cl
	VP1		R2	R2	R2	R2	R2	R2	R1	R1	R1	R1	R1	R1	R1	R2	R1	R1	R2	R2	R2	R1	R1	R1	R1	R1	R2	R1	R1
	AP6		12	12	12	12	12	12	Ξ	Ξ	П	Π	Π	IS	IS	12	п	12	12	12	110	п	IS	IS	п	112	12	Π	Ξ
	VP4	P[1]	P[4]	[6]	[8]d	P[10]	P[14]	P[14]	P[8]	P[8]	[8]d	P[8]	P[11]	P[19]	P[19]	[9]d	[8]d	[8]d	P[11]	P[11]	P[15]	[9]d	[/]J	[/]J	P[25]	P[25]	P[4]	[6]	P[6]
	VP7	85	G8	G8	89	89	G8	85	69	69	6D	69	69	69	6D	G10	G10	G10	G10	G10	G10	G11	G11	G11	G11	G11	G12	G12	G12
	STRAIN NAME	RVA/Cow-tc/THA/A5-13/XXXX/G8P[1]	RVA/Human-wt/DEU/GER1H-09/2009/G8P[4]	RVA/Human-wt/COD/DRC86/2003/G8P[6]	RVA/Human-wt/COD/DRC88/2003/G8P[8]	RVA/Human-tc/IND/69M/1980/G8P4[10]	RVA/Human-wt/HUN/BP1062/2004/G8P[14]	RVA/Sheep-tc/ESP/OVR762/2002/G8P[14]	RVA/Human-wt/BEL/B3458/2003/G9P[8]	RVA/Human-tc/USA/WI61/1983/G9P1A[8]	RVA/Human-wt/USA/OM46/1998/G9P[8]	RVA/Human-wt/USA/OM473/2000/G9P[8]	RVA/Human-tc/IND/116E/1985/G9P[11]	RVA/Human-wt/IND/RMC321/1990/G9P[19]	RVA/Human-wt/IND/mani-97/2006/G9P[19]	RVA/Human-wt/IND/mani-265/2007/G10P[6]	RVA/Human-wt/NGA/6717ARN/2002/G10P[8]	RVA/Human-wt/CIV/6755ARN/2002/G10P[8]	RVA/Human-wt/IND/N155/XXXX/G10P[11]	RVA/Cow-xx/CHN/DQ-75/2008/G10P[11]	RVA/Sheep-tc/CHN/Lamb-NT/XXXX/G10P[15]	RVA/Human-wt/ECU/EC2184/2005/G11P[6]	RVA/Pig-tc/MEX/YM/1983/G11P9[7]	RVA/Pig-tc/VEN/A253/1988/G11P9[7]	RVA/Human-wt/BGD/Dhaka6/2001/G11P[25]	RVA/Human-wt/NPL/KTM368/2004/G11P[25]	RVA/Human-tc/PHL/L26/1987/G12P[4]	RVA/Human-wt/BGD/Dhaka12-03/2003/G12P[6]	RVA/Human-wt/BGD/Matlab13/2003/G12P[6]

CORD A THE NA MET						GENOTYPES	YPES					Ē
S I KAIN NAME	VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5	KEF.
RVA/Human-wt/BGD/RV161/2000/G12P[6]	G12	P[6]	12	R2	C2	M2	A2	N2	T2	E1	H2	(73)
RVA/Human-wt/BGD/RV176-00/2000/G12P[6]	G12	P[6]	12	R2	C2	M2	A2	NZ	T2	9 3	H2	(73)
RVA/Pig-wt/IND/RU172/2002/G12P[7]	G12	P[7]	IS	R1	C1	M1	A1	IN	T1	E1	H1	(31)
RVA/Human-wt/BEL/B4633/2003/G12P[8]	G12	P[8]	11	R1	C1	M1	A1	IN	T1	E1	H1	(73)
RVA/Human-wt/BGD/Dhaka25-02/2002/G12P[8]	G12	P[8]	11	R1	C1	M1	A1	N	T1	E1	H1	(73)
RVA/Human-tc/THA/T152/1998/G12P[9]	G12	P[9]	I3	R3	C3	M3	A12	N3	Т3	E3	9H	(73)
RVA/Horse-wt/ARG/E403/2006/G14P[12]	G14	P[12]	12	R2	C2	M3	A10	NZ	Т3	E2	H7	N.P.
RVA/Cow-xx/ARG/B383/1998/G15P[11]	G15	P[11]	12	R5	C2	M2	A13	NZ	9L	E12	Н3	(55)
RVA/Cow-tc/IND/Hg18/XXXX/G15P[21]	G15	P[21]								E2		(9L)
RVA/Mouse-tc/XXX/EHP/1981/G16P[20]	G16	P[20]					A7			ĽΞ		(25)
RVA/Turkey-tc/IRL/Ty-1/1979/G17P[17]	G17	P[17]	14					N4		E4		(65)
RVA/Pigeon-tc/JPN/PO-13/1983/G18P[17]	G18	P[17]	14	R4	C4	M4	A4	N4	T4	E4	H4	(36)
${\tt RVB/Rat-tc/USA/IDIR/1984/GIP[X]}^b$	G1b											(63)
${\rm RVB/Human-wt/CHN/WH-1/2002/G2P[X]}^b$	G2b											(101)
${\rm RVB/Human-wt/BGD/Bang117/2003/G2P[X]}^{b}$	$G2^{b}$											(86)
${\rm RVB/Cow-wt/IND/DB176/2001/G3P[X]}^b$	G3b											(10)
$\mathrm{RVC/Pig\text{-}tc/GBR/Cowden/1982/G1P[1]}^{\textit{b}}$	G1b	$P[1]^b$										(71)
${\rm RVC/Cow\text{-}tc/JPN/Shintoku/1991/G2P[3]}^b$	G2b	$P[3]^b$										(68)
$RVC/Human-tc/GBR/Bristol/1998/G4P[2]^{\emph{b}}$	$G4^b$	$P[2]^b$										(35)
${\rm RVC/Human-} wt/{\rm BGD/BS347/2005/G4P[2]}^b$	G4b	$P[2]^b$										(66)
RVD/chicken-wt/DEU/05V0049/2005/GXP[X]												(87)

^aOnly the partial VP8* coding region of the VP4 sequence of P[22] strains is currently available.

benotypes are provisional. Guidelines about the classification of RV strain belonging to RVB and RVC, will be determined in the near future by the RCWG.

 $^{^{}c}$ Due to a typographic error, the NSP3 genotype of strain NIC522, was previously misidentified as T2 (5).

An open space refers to: i) genotype not known, as sequencing has not been performed, or ii) genotypes have not yet been established for non-group A RVs. Abbreviation: N.P., not published.

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Table 3

Hypothetical examples of nomenclature for RV vaccine strains and laboratory generated/engineered strains.

COTO A TAN MANAGE					Ð	GENOTYPES	PES					9
SIKAININAME	VP7	VP4	VP6	VP1	VP2	VP3	NSP1	NSP2	NSP3	NSP4	NSP5	KEF.
RVA/Env/CHE/River-Swiss/1998/G3P[X] ^a	G1											(2)
${\rm RVA/Simian-lab/USA/SA11-tsE/XXXX/G3P[2]}^{b}$	G3	P[2]	12	R2	CS	M5	A5	N2	T5	E2	H5	XX
RVA/Cow-lab/GBR/PP-1/1976/G3P[7] ^C	G3	P[7]					A3			E8		(21)
${\tt RVA/Labstr/USA/RRV-E4/1996/G3P[20]}^d$	G3	P[20]	12	R2	C3	M3	A9	N2	Т3	E3	9Н	(44)
RVA/Labstr/USA/SA11-huN2/2010/G3P[2] ^e	G3	P[2]	12	R2	C5	M5	A5	N2	T5	E2	H5	(82)
${\rm RVA/Vaccine/USA/RotaTeq-WI79-9/1992/G1P7[5]}^f$	G1	P7[5]	12	R2	C2	M1	A3	N2	Т6	E2	Н3	(53)
${\rm RVA/Vaccine/USA/RotaTeq-SC2-9/1992/G2P7[5]}^f$	G2	P7[5]	12	R2	C2	M1	A3	N2	Т6	E2	Н3	(53)
${\rm RVA/Vaccine/USA/RotaTeq-WI78-8/1992/G3P7[5]}^f$	G3	P7[5]	12	R2	C2	M2	A3	N2	T6	E2	Н3	(53)
${\rm RVA/Vaccine/USA/RotaTeq-BrB-9/1996/G4P7[5]}^f$	G4	P7[5]	12	R2	C2	M2	A3	N2	T6	E2	Н3	(53)
${\rm RVA/Vaccine/USA/RotaTeq-WI79-4/1992/G6P1A[8]}^f$	99	P1A[8]	12	R2	C2	M2	A3	N2	Т6	E2	Н3	(53)
RVA/Vaccine/USA/Rotarix-RIX4414/1988/G1P1A[8]	G1	P1A[8]	11	R1	Cl	M1	A1	N1	Т1	E1	H1	N.P.

^aHypothetical name of a RV strain identified in a river in Switzerland (2).

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 $^{^{}b}$ strain SA11-tsE is a temperature sensitive RV strain (SA11) generated using chemical mutagenesis.

^CStrain PP-1 is a bovine RV strain wish has been passages several times in the heterologous pig model (21)

Hypothetical name of a RV strain generated using in vitro reassortment in cell culture, possessing an RRV-like gene background with the VP4 gene (genotype P[20]) of the murine RV strain EHP (44).

Hypothetical name of a RV strain generated using reverse genetic techniques, possessing an SA11-like gene background with the NSP2 gene (genotype N2) of the human RV strain DS-1 (85).

f. Hypothetical names of the 5 reassortant RV strain present in the RotaTeq vaccine (53).

 $[\]ensuremath{\mathcal{E}}$ Hypothetical name of the RV strain present in the Rotarix vaccine.

An open space refers to the genotype not being established/determined.