



## Best practice guidelines on reporting in molecular genetic diagnostic laboratories in Switzerland

1.	Scope and application of these Guidelines.....	1
2.	General.....	2
3.	Laboratory Identification, Signature and Administrative elements.....	2
4.	Patient Identification.....	3
5.	Restate in some form the clinical question being addressed .....	3
6.	Specify the tests used .....	3
7.	Present the laboratory results in a brief unambiguous form .....	4
8.	Interpretation .....	4
9.	Answer the question in a concise and clear way .....	5
10.	Further tests and/or information .....	5
11.	Requirement for genetic counselling.....	5
12.	Interim reports .....	6
13.	Reporting multiple patients.....	6
14.	Disclaimers.....	6
15.	References .....	7
16.	Comments concerning laboratory accreditation (EN ISO/IEC 17025).....	7
17.	Check-list for “standard report”: .....	8
18.	Standard report based on these guidelines .....	8

### 1. Scope and application of these Guidelines

- 1.1. This text presents Best Practice Guidelines for Swiss laboratories reporting molecular genetic diagnostic testing of constitutional mutations.
- 1.2. The aim of the guidelines is to improve the quality of reporting in Switzerland and to help laboratories to provide the most understandable and complete reports of their analyses.
- 1.3. The guidelines are modified with permission from the draft guidelines on Reporting of the European Molecular Quality Network (EMQN, [www.emqn.org](http://www.emqn.org)). The EMQN has no responsibility for this modified version. The guidelines also take account of the ISO/IEC 17025 norm and of the NCCLS “Molecular Diagnostic Methods for Genetic Diseases; Approved Guideline” (MM1-A, Vol. 20 No. 7, 2000).
- 1.4. Laboratories following these Guidelines in essence may state “Laboratory reports are produced according to the Best Practice Guidelines of the Swiss Society of Medical Genetics”. Any Laboratory who includes this statement in external documentation is required to inform the Society (General Secretary) by writing. Laboratories are free within reason to modify elements of the guidelines if they feel this is appropriate; the Committee of the Society alone can judge whether such modifications remain within the essence of the Guidelines.

## 2. General

- 2.1. Reports are specific formal documents from the laboratory to the referring doctor, recording the outcome of molecular genetic investigations on a patient. Their principal aim is to provide a clear, concise, accurate, fully interpretative and authoritative answer to a clinical question.
- 2.2. Reports must in particular be understandable by medical professionals who may have little background in genetics and who are unable to correctly or fully interpret genetic data.
- 2.3. The interpretation of molecular genetics results depends entirely on the context (see 6.1).
- 2.4. Reports should not extend beyond one side of a page, insofar as is possible.
- 2.5. The conclusion must be evident (e.g. bold).
- 2.6. Reports should be typed, word-processed or created by computer. Hand-written reports are not acceptable.
- 2.7. Integrated laboratory computer systems often have reporting modules which simplify report writing by use of coded or automatic text. Careful thought needs to be put into setting these systems up so that the coded text is meaningful, accurate, appropriate and adaptable to different situations.
- 2.8. Reports should be sent to the referring doctors, medical institution or medical genetics laboratory. If the latter has requested in writing that copies be sent to other health care professionals, this should be done. If the laboratory feels sending copies is inappropriate (e.g. in HD predictive testing, APOE genotyping etc.) this should be discussed with the referring doctor.
- 2.9. The result must be archived in the patient's file in the laboratory (electronically or on paper). As molecular genetics results have implications for relatives of the patient tested, thirty years (one generation) is proposed as the **minimum** archive period; *ad eternam* is preferable.

## 3. Laboratory Identification, Signature and Administrative elements

- 3.1. The Laboratory issuing the report should be clearly identified, with full contact details. The report should carry a title (e.g. "Result of genetic analysis") and be dated.
- 3.2. The page number and total number of pages should be indicated on every page.
- 3.3. If any part of the analysis for which results are presented is performed in an external lab, it is essential to indicate this on the report and to clearly indicate which results come from which laboratory. It is strongly recommended that the original report is transmitted in its original form.  
If your laboratory is accredited and the external laboratory is not, it is essential to indicate this fact.
- 3.4. The sample nature and date of reception should be mentioned.
- 3.5. Unless the preanalytical phase is assured by the laboratory, the report should indicate that the results apply only to the supplied sample.
- 3.6. The name of the person (doctor, laboratory) requesting the analysis should be indicated.
- 3.7. Reports should be signed by the laboratory director (or another FAMH Specialist in Medical Genetic Analyses or other title-holder authorized for the analysis).
- 3.8. It is recommended that reports are co-signed or initialled by a second person who has interpreted the result (usually the person who has performed the analysis).
- 3.9. The name, function or other identification of all signatories must be given.
- 3.10. It is preferable that reports be signed manually, not electronically.

#### 4. Patient Identification

- 4.1. Even though many tested individuals are in good health, for simplicity the word “patient” is recommended.
- 4.2. Patients should be identified on reports by at least two items of information, most commonly full name and date of birth. Inclusion of laboratory accession number is strongly recommended.
- 4.3. When several reports are written on different members of a family or when one report concerns several individuals, it is recommended to include pedigree or family number or equivalent, and/or to indicate the family relationships clearly. Whenever possible, it is recommended to issue separate reports for each individual, carrying only data essential for the interpretation, to preserve confidentiality (see 14).
- 4.4. Foetal samples (CVS, amniocytes etc.) should be clearly distinguished from those of their mothers (cytogenetics labs commonly identify such samples with the mother’s name, which is not acceptable for DNA).

#### 5. Restate in some form the clinical question being addressed

- 5.1. **The interpretation of molecular genetics results depends entirely on the clinical context.** Therefore, reports should explicitly restate the clinical question being asked (or if the referral form is ambiguous, what the question is that is being answered). This usually comprises at least the following three elements:
  - The disease/marker being tested (e.g. fragile-X syndrome, cystic fibrosis)
  - The request being made (e.g. diagnostic confirmation, carrier status)
  - The indication - why the request is being made (e.g. positive family history).
- 5.2. In the absence of clinical information, the laboratory should indicate that the accuracy of the interpretation depends on that of the assumed question.
- 5.3. If space permits, re-state any additional information on the referral form which has a bearing on the clinical question.  
*Reminder: accredited labs must clearly distinguish whether or not this indication/question is part of the scope of the accreditation.*

#### 6. Specify the tests used

- 6.1. Indicate the material that has been tested (e.g. “EDTA blood”, “cultured amniocytes”, “purified DNA”). If the position of sampling is relevant to the quality of the result (e.g. muscle biopsy, tumour/normal tissue) this should be indicated.
- 6.2. Include brief technical details about the tests used in the analysis. This is of particular importance in situations where other laboratories may have to analyse relatives of your reported patient or where the patient may in the future undergo further investigation following a negative result. It is particularly useful to state which test is used when a number of alternatives are in established usage (e.g., ARMS, fluorescent OLA or restriction analysis to detect CF mutations).
- 6.3. Give full details of the extent of the tests (e.g. which exons screened for deletions in DMD, which mutations looked for in CF etc). Again, this is particularly important when reporting negative results.
- 6.4. When reporting mutation detection studies, mention the method(s) used. For techniques which are not entirely sequence-specific, the interpretation should state "...consistent with...". Methods include:

##### Sequence-specific methods

direct sequencing  
creation of a restriction site  
ARMS  
ASO hybridisation  
OLA

##### Non sequence-specific methods

SSCA  
destruction of a restriction site  
sizing  
PTT  
DGGE.

## 7. Present the laboratory results in a brief unambiguous form

- 7.1. The results should include sufficient precise data to be fully interpretable to other laboratories, without becoming a scientific paper.
- 7.2. Use of "+" and "-" in reporting mutations is open to misinterpretation and should be avoided.
- 7.3. Nomenclature should be meaningful, unambiguous and consistent. The HUGO standard mutation nomenclature system ([den Dunnen & Antonarakis, Hum Genet 109\(1\): 121-124, 2001](#)) is recommended by the SSGM as it reduces the potential for ambiguity when reading reports issued by other labs. Note that the base/codon numbering system, although unambiguous, frequently differs from systems that were in place before 1998.
- 7.4. If for some reason other nomenclature is adopted, the following points should be considered:
  - For mutation studies, letter codes are most straightforward. Avoid symbols which may not exist on all keyboards/in email (e.g. use F508del, not Greek delta).
  - Avoid mixing code/numbering systems on different reports.

If the HUGO system is not used, a key should be used to avoid confusion and to allow other laboratories to accurately interpret your report.
- 7.5. For microsatellites and other length polymorphisms, the most commonly used scoring system is to assign numbers with "1" representing the largest allele. Specify the scoring system used (e.g. "alleles are numbered from largest to smallest").

### *Family studies (see also 14)*

- 7.6. A table and/or annotated pedigree can convey complex information much more concisely than text. This format is particularly recommended for linked-marker studies.
- 7.7. The pedigree should include sufficient information to unambiguously identify the family (include family/ pedigree number) and to distinguish each relevant person.
- 7.8. Pedigree diagrams should include only those individuals relevant to the interpretation. The confidentiality of information of relatives of the patient being reported must be a consideration - see 14.
- 7.9. Where pedigree diagrams display linked-marker haplotypes, the marker order presented should accurately reflect marker order on the chromosome or around the gene. An indication of orientation should be made to avoid potential confusion. We recommend p-telomere to q-telomere.

## 8. Interpretation

- 8.1. The report must provide a **full and clear interpretation** of molecular genetic test results. Reports are destined to be read by a variety of professionals involved in the care of the patient, many of whom will be unable to fully interpret genotyping results.
- 8.2. Some laboratories may feel pressurised not to provide full interpretation by clinicians who prefer to interpret genotyping results themselves. This pressure should be resisted - if the clinicians do not want to read the interpretation, they can ignore that section of the report. The inclusion of an interpretation of results, and not just the result itself, is a responsibility of FAMH Specialists in Medical Genetic Analysis.
- 8.3. In order to provide a full interpretation, genotyping results must be reviewed in the context of the relevant clinical and family information available. The report should restate briefly any such information which is considered in the final interpretation (this may have been done at the beginning of the report; see 6. The information may include the following:
  - Relationship between the patient and the index case where there is a family history of the disease.
  - Ethnic background where relevant (e.g. CF)
  - Other laboratory investigations (e.g. CPK results in DMD)
  - Unusual or suspicious clinical picture (e.g. foetal echogenic bowel in CF).

- 8.4. In the case of negative results, it is important to provide an estimate of the diagnostic sensitivity (ie the proportion of affected individuals likely to be detected). Sensitivity estimates may be influenced by information supplied on the referral form (see 7.3). It can be useful to provide a key reference to support sensitivity estimates when appropriate, but the report should not become a scientific discussion.
- 8.5. In the case of positive results, it is often important to provide an estimate of diagnostic specificity, which indicates the risk of a false-positive result (typically, in late-onset diseases or in case of reduced penetrance).
- 8.6. When appropriate, genetic carrier risks should be stated (e.g. “the patient’s residual risk of carrying a CF mutation is ...”). Risk estimates are usually most appropriately based on Bayesian calculations and are most commonly calculated “by hand”.

## 9. Answer the question in a concise and clear way

- 9.1. The final answer to the clinical question is a statement of the interpretation of the genotyping results taking into account any appropriate additional information supplied. Wherever possible this should be expressed in a simple concise statement.
- 9.2. It is recommended that laboratories **highlight** this conclusion (bold, underline, large font, text in a box etc). Clinicians familiar with the report format (or in a hurry) will focus on this “bottom line” and ignore the “blurb”. For this reason careful thought must be given to wording so that the statement is accurate and not open to misinterpretation. Appropriate phrases include:
  - “This patient shows no evidence of a fragile-X expansion”,
  - “This patient is a CF carrier”, “low risk of being a carrier”,
  - “The absence of the mutation excludes the diagnosis”,
  - “This negative result does not formally exclude the diagnosis but renders it highly unlikely”.

*Disease-specific suggestions can be found at [www.emqn.org/bpguidelines.htm](http://www.emqn.org/bpguidelines.htm).*
- 9.3. In particular, remember that negative results (“no mutation detected”) can easily be misinterpreted by non-specialists as exclusions.

## 10. Further tests and/or information

- 10.1. Indicate if further tests could be undertaken to improve the accuracy or scope of the interpretation. This may include tests for additional disorders or additional tests to more fully investigate the disease in question.
- 10.2. If the additional tests suggested are not performed “in-house”, alternative specialist laboratories where the DNA may be sent can be proposed.
- 10.3. Suggest any other information which could be supplied or arranged by the referring clinician which might improve the accuracy of your interpretation (e.g. arranging testing of the index case in a family to confirm a diagnosis or to determine which mutations are present).

## 11. Requirement for genetic counselling

- 11.1. The report should carry the reminder to the referring doctor that “genetic tests should be accompanied by genetic counselling” (or similar).
 

*Note that at present in Switzerland it would be incorrect to say “must be accompanied by” nor “counselling by an FMH Specialist in Medical Genetics is essential”.*
- 11.2. It is essential that all positive (abnormal) results should carry the suggestion of counselling.
- 11.3. In certain cases (prenatal diagnosis, presymptomatic testing, or results with major implications for other family members) it is appropriate to indicate that “this result and its implications should be transmitted only in a specialized genetic consultation” (or similar).
- 11.4. Family follow-up. When a new diagnosis is made (positive result in a diagnostic confirmation) it may be appropriate to state specifically that the result has “potentially important implications for other family members” or equivalent.

- 11.5. It must never be stated that prenatal or presymptomatic diagnosis is “indicated” or “necessary”. The role of the laboratory does not go beyond stating that diagnosis “would be possible if desired”.

## 12. Interim reports

- 12.1. It may in some circumstances be useful to issue a report before all studies are complete (e.g. when indicative preliminary results have been obtained but a long delay is expected before the final results will be ready). Interim reports should be clearly marked as such and should be worded to avoid misinterpretation of their status. Thus, phrases or summary statements appearing to give a definitive result should not be used.
- 12.2. It should be clearly stated which analyses are still underway.
- 12.3. The definitive report should clearly state which are the new results, and should include a general conclusion taking account of all results.

## 13. Reporting multiple patients

- 13.1. As a general rule, each unrelated patient should be reported on a separate and unique document, since the reports will ultimately be filed in individual patient or family files (as well as for reasons of confidentiality).
- 13.2. When several family members are analysed simultaneously, policies vary as to whether they should be reported on the same or on different reports. This will depend on the disorder and the nature of the analysis as the following situations illustrate:
- Huntington’s (and comparable) predictive test results **must always** be reported on separate, individual reports.
  - Linked-marker studies only make sense in the context of alleles inherited by several family members, which must be included in the report. It is recommended to restrict the number of individuals reported to only those essential for accurate analysis, and to include an interpretation and final risk only for one person per report.

Uncertainty about whether or not to report several relatives on the same report might be resolved by considering:

- is the answer to an individual’s clinical question dependent upon stating information about other family members?
  - since a copy of the report may be filed in the patient notes of each individual reported, what are the consequences of any of those individuals having access to information about other family members?
- 13.3. If a couple undergo carrier testing for CF (or other recessive disorders) prior to embarking on pregnancy, the information they require is the risk to their foetus. The test results for one partner must be interpreted in light of the other partner’s results and it is common practice to report both individuals together. However, some laboratories are uneasy about this (the couple may separate) and issue separate reports but with cross references to the partner’s results.

We recommend issuing separate reports, with each indicating the name of the partner and a conclusion “the risk that a child of this couple be affected by CF is 1 in ...”.

## 14. Disclaimers

- 14.1. Mention only where appropriate the possibility of errors due to factors beyond the control of the laboratory (e.g. the risk of “non-paternity” and the need for family relationships at stated on the referral forms being correct).
- 14.2. In indirect (linkage) analyses, it is sometimes advisable to state that the “accuracy of the result depends on the clinical diagnosis and the assumption that gene X is responsible for disease” (or similar).
- 14.3. It is neither necessary nor desirable to mention the possibility of laboratory error or sample mislabelling on every report. However, laboratories might wish to add a note of caution when reports are based on DNA samples or reports sent from another laboratory.

- 14.4. It is suggested that all reports carry a standard phrase indicating that “this report cannot be copied or reproduced, except in its totality”.

## **15. References**

- 15.1. References should be given when published data have a bearing on the interpretation or risk calculation. In general references are only necessary when the data are newly published or present information which is not widely known or accepted. When different publications present conflicting data, it is important to specify which has been used as the basis for your interpretation.
- 15.2. Include enough information to allow the reader to obtain the reference themselves, (e.g. Rousseau et al. *Am. J. Hum. Genet.* 55: 225 (1994), rather than just Rousseau et al. 1994).

## **16. Comments concerning laboratory accreditation (EN ISO/IEC 17025)**

- 16.1. These Guidelines have been designed to help fulfil the requirements of the Swiss Accreditation Service (SAS) for accreditation according to the cited European norm. Although the SSGM cannot formally guarantee that such reports will automatically fulfil the requirements of the SAS, all laboratories who have accredited or are considering accrediting medical genetic analyses are strongly encouraged to implement the Guidelines, for their own benefit as well as for a better service.
- 16.2. Accredited laboratories need to state what elements of the report are covered by the accreditation (for example, not the sample, not the indication, not the Commentary etc). Similarly, results of analyses which are not accredited must be indicated (e.g. by a symbol).

---

## 17. Check-list for “standard report”:

Laboratory Identifiers

Title, date

**Name of patient** (at least two identifiers; date of birth, sample number, etc)

Indication for testing or question to be answered

Test performed, mutations tested, sensitivity

Methods used (in brief)

Result (formal genotype)
--------------------------

### Interpretation of result in simple language

Remarks on sensitivity, specificity, context

Requirement for counselling and/or further testing

Signature of lab director, visa/signature of second person

Laboratory’s Standard phrase concerning reproduction of report and scope of results.

## 18. Standard report based on these guidelines

see following page; note that no requirements of layout are imposed.

**The Swiss Hospital**  
 Division of Genetics  
 Laboratory of Molecular Genetics  
 Our Address  
 Tel (+41) 012 34 56 789, Fax 012 34 56 780  
 email [the.geneticist@switzerland.ch](mailto:the.geneticist@switzerland.ch)



**Report of molecular genetic investigations**

City, 12-12-1602

*Patient(s):* **MENDEL Gregor (22-7-1822; # 00001)**

*Indication:* Clinical suspicion of autosomal dominant achocolataemia.

<i>Analyses:</i>	DNA extraction. Analysis of the most common mutations of the gene <i>CHOC1</i> , by PCR and sequencing of exon 10 (reference: <i>Eur J Choc Biol</i> 1 123-456).	<i>Material tested:</i>	EDTA blood.
		<i>Sample received :</i>	1-1-2002

*Result:* **No *CHOC1* mutations detected.**

*Interpretation:* **The absence of any mutations in exon 10 makes the diagnosis very unlikely, without formally excluding it (99% of patients have a mutation in this exon).**

*Remarks:* Further very rare mutations could be analysed on request.

Signature

Gene TESTER Ph.D.  
 FAMH specialist in medical genetic analysis  
 Laboratory Director

signature/initials

Analyses performed by: XYZ

*Analysis requested by* Dr A. Medic, Switzerland

*Copy to* -

*Because of their complexity and their potential implications for other family members, all genetic tests should be accompanied by genetic counselling.*