WORLD FEDERATION OF HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HÉMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA

WFH INTERNATIONAL EXTERNAL QUALITY ASSESSMENT SCHEME (IEQAS) PROGRAM

PARTICIPANTS' MANUAL & GENERAL INFORMATION 2025 – 2026

3rd Floor, Pegasus House, 463A Glossop Road, Sheffield S10 2QD, U.K.
Tel: +44 (0)114 267 3300
E-mail: IEQAS ieqas@wfh.org
Web site: www.ukneqasbc.org

BACKGROUND

The World Federation of Hemophilia (WFH) improves and sustains care for people with inherited bleeding disorders around the world. The WFH has been supporting people with inherited bleeding disorders and treatment for over 60 years.

The WFH International External Quality Assessment Scheme (IEQAS) was launched in 2004 to monitor and improve laboratory performance in Hemophilia Treatment Centres (HTCs) worldwide. Laboratories can participate in this scheme to assess their quality assurance systems and the reliability of their test results.

IEQAS improves and standardizes laboratory diagnosis by auditing the effectiveness of the internal quality assurance systems in place and giving measures of the laboratory's competence.

The scheme is operated by the United Kingdom's National External Quality Assessment Scheme (UK NEQAS) for Blood Coagulation, based in Sheffield, which has been inspected by the United Kingdom Accreditation Service Ltd (UKAS) and which has been granted full accreditation to ISO 17043 for all listed tests.

The mandate of the WFH IEQAS is to provide an external quality assessment (EQA) for tests of blood coagulation and to promote high standards of performance and practice. EQA, together with internal quality control (IQC) procedures, are vital components of overall laboratory quality assurance. In addition, the WFH IEQAS provides an advisory service to participants through exchanges on lab diagnosis, including a participants' meeting during the biennial WFH World Congress and onsite/virtual visits to provide training, as needed.

The WFH IEQAS Committee is responsible for overseeing the International External Quality Assessment Scheme (IEQAS) program. The committee is comprised of an independent chair appointed by the WFH, the Scheme program director, IEQAS program staff in the Sheffield Teaching Hospitals (host institution), and WFH staff and volunteers. The IEQAS Committee oversees all operational aspects of the program, reviews participation in the scheme, analyses results, monitors global laboratory performance, and provides advisory support for centres registered on the scheme.

REGISTRATION

A review process ensures that WFH evaluates IEQAS applications. Laboratories are chosen based on their involvement in the diagnosis of hemophilia and other related bleeding disorders. Generally, there is one main reference laboratory that is enrolled in IEQAS from each country. In some countries, several laboratories may be enrolled in the scheme. The WFH is prepared to sponsor the enrolment fee of certain centres in low and low middle income countries which are involved in other WFH programs.

Enrolment runs from February to the following February, and centres cannot join mid-year. IEQAS participation forms must be received by the WFH by February in order to be reviewed and included in the scheme for a year. Centres new to the scheme must submit a completed laboratory questionnaire and participation form by the deadline set by the WFH.

PARTICIPATION

Samples for blood coagulation tests are distributed to participating laboratories around the world. The WFH IEQAS ensures the protection of participants' confidential information but does share information with the WFH for laboratories whose participation is sponsored.

WFH IEQAS participants can select which tests they will complete and provide results for. It is recommended that participants register for all tests that their laboratory offers. The www.ukneqasbc.org website can be used for online result submission and to view survey reports. Participants are provided with a password in order to access the result entry pages of the website.

PERSONNEL

Members of the UK NEQAS team include:

Dr. S Kitchen	Scheme Director (steve.kitchen1@nhs.net)
Dr. I Jennings	Scheme Manager
Mrs. D P Kitchen	Scheme Program Scientist
Mrs. A Lowe	Scientific Lead for Haemophilia programmes
Mr. C Reilly-Stitt	Scheme Deputy Manager

Postal address:	3rd Floor Pegasus House, 463A Glossop Road, Sheffield, S10 2QD U.K.
Telephone:	+44 (0)114 267 3300
E-mail:	ieqas@wfh.org
Web site:	www.ukneqasbc.org

TESTS COVERED BY THE WFH IEQAS PROGRAM:

The WFH IEQAS surveys are distributed three times per year, typically in March, July, and November.

All surveys usually include:

Prothrombin Time (PT)
Activated Partial Thromboplastin Time (APTT)
FVIII assay
FIX assay

Two of the three surveys include:

von Willebrand factor antigen assay
VWF:Ristocetin cofactor/VWF activity assays

One out of the three surveys include:

Two other factor assays so that FII, FV, FVII, FX and FXI assays are all assessed at some stage, along with fibrinogen.

EQA for genetic testing, in relation to inheritable bleeding disorders, is available through an international EQA program. For details, contact neqas@coageqa.org.uk.

SUPPLEMENTARY EXERCISES

Supplementary exercises are carried out to address other issues in haemostasis testing. Past exercises have included a FVIII inhibitor exercise, APTT mixing studies, and assays for Emicizumab. Reports are circulated to participating centres and data is presented back to participants at the biennial participant's meeting.

REPORTS

Individual reports for each survey are sent approximately two weeks after the closing date for the respective survey. Reports are made available as online PDF documents. In the event that a participating centre submits their results after the deadline, they will receive a "retrospective report". Please submit all late results to ieqas@wfh.org

PERFORMANCE ANALYSIS

Performance is determined by the comparison of individual laboratory results with the target value for each test. Target values and median used for this test are typically determined prior to the survey when the same samples were tested by participants in the UK NEQAS Blood Coagulation Programme.

The UK NEQAS BC Programme has over 1000 participants, which means that the peer groups are large and the data is therefore robust enough for assessment of individual centre results. In general, the median results obtained by the WFH IEQAS participants are very similar to the median determined from the UK NEQAS BC group. As the number of participants in the WFH IEQAS program is relatively small, analysis of the minor reagent groups is only made meaningful by the use of the UK NEQAS BC values to define the target ranges. Use of the median avoids the effect of outlying results which can significantly impact on mean values in some cases.

Where consistent reagent or method-related differences have been identified, participants' results are assessed against their 'peer-groups' within UK NEQAS BC Programme. However, this only occurs if the number in that group is sufficient to be statistically valid.

For PT and APTT

For PT and APTT, the percentage deviation of each individual laboratory's results from the reagent and overall medians are calculated, with the following criteria for performance applied:

Performance is considered "*within consensus*" if the deviation is <15% from:

- ✓ the **reagent median** if the number of users of that reagent is equal to or greater than 10 *or*
- ✓ the **overall median** if the number of users of the reagent is less than 10.

Results >15% deviation from the median are considered "*outwith consensus.*"

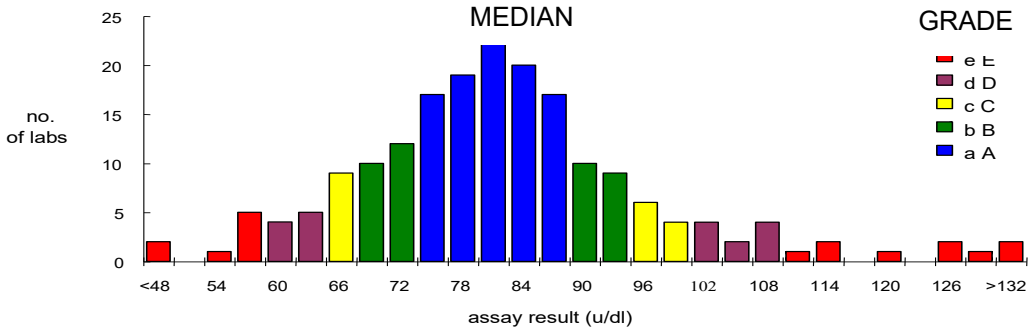
Factor Assays

For Fibrinogen assay, Clauss method results are assessed against the overall Clauss method median, with results >15% from this median considered outwith consensus. Multifibrin U users are assessed separately.

For other factor assays, WFH IEQAS distributes samples with factor concentrations covering the wide range encountered in clinical practice. A ranked grading analysis is used to evaluate performance, alongside z scores.

For ranked grading analysis, the overall consensus median is taken as the central reference point or “target value”. Individual results are ranked into five unequal quantiles above and below the median, each quantile being designated by a letter depending on ranked distance from the median:

Group A: *The nearest 25% of results above (A) and below (a) the median (i.e. 50% of results);*
Group B: *The next 10% of results above (B) and below (b) the median (i.e. 20% of results);*
Group C: *The next 5% of results above (C) and below (c) the median (i.e. 10% of results);*
Group D: *The next 5% of results above (D) and below (d) the median (i.e. 10% of results);*
Group E: *The 5% of results furthest from the median, above (E) and below (e) (i.e. 10% of results).*



Grades below the median are shown in lower case, and above the median in upper case, to aid in assessment of bias.

Performance is based on grades obtained in two consecutive exercises for any particular test. *Performance "outwith consensus"* is defined as a combination of a C (or ‘c’) grade together with an E (or ‘e’) grade, or any combination of D (or ‘d’) and E (or ‘e’) grades (e.g. cE, ec, Dd, de, ED and EE in consecutive distributions of that particular assay).

Persistent "outwith consensus" performance is defined as two consecutive *"outwith consensus"* performances. This will arise from three consecutive performances with the following combinations of grades (upper case only shown for example purposes):

DDD, DED, ECE, EEC, DDE, DEE, EDD, EED, CEE, EDE, EEE

A non-return for a registered test will be graded as 'F' and taken as equivalent to an E grading. Thus, designations which include 'F' grades are based on performance over two or three exercises, respectively.

Z scores

Currently results are scored using the a-e grading system as explained above. We also use z scores, as an additional measure of assay performance, and we show both a-e grade and z scores on the reports. The z score is calculated as follows. The central reference point is taken as the overall consensus median. The robust mean and SD are calculated by statistical exclusion of outlying results. The z-score is calculated as

[result – mean] / SD

A z-score of >+/-2 is considered outwith consensus, with a warning flag; a z-score of >+/-3 is considered outwith consensus with an action required flag. 'Action required' is also applied to two consecutive z scores >+/-2. Two consecutive surveys with z scores >+/-3, or 3 surveys with z scores >+/-2 will be considered persistently outwith consensus

The terminology "action" and "warning" is derived from ISO13528 guidance on use of z scores in proficiency testing programmes. We suggest that an "action required" flag would prompt a laboratory to review their assay results and decide whether further action is warranted; in particular, the clinical implication of their performance should be considered. A "warning" flag indicates a result outlying from the median, which should be monitored in future surveys.

In instances of results that are currently considered outwith consensus using the a-e grading system the z scores should also be reviewed to enable users to decide what further action may be required.

In some cases, significant differences have been noted between different methodologies. Where this occurs on a consistent basis, separate analysis of the groups is carried out, using medians specific to each method group. However, the system is only effective if the number of participants is greater than 20; consequently, grading analysis is not applied to groups of results from fewer than 20 centres.

At present, the following groups are analysed separately (groupings are regularly reviewed):

- Factor VIII:C (One stage and chromogenic assays)
- VWF Ristocetin Cofactor (VWF activity ELISA, Aggregometry, individual Latex assays, chemiluminescence.

If results of screening tests are outwith consensus on three consecutive occasions (including failure to return results), or results from factor assays are persistently outwith consensus, a letter of concern with an offer of assistance is sent by the Scheme Director to the head of the sponsored laboratory. For WFH sponsored centres, these concerns can also be communicated with the chairs of the WFH Laboratory Science and IEQAS committees.

NON-RETURN OF RESULTS

The aim of the program is to help centres which need support and guidance; therefore, there should be a sense of responsibility for sponsored laboratories to maintain good communication with the WFH.

A follow-up letter is sent after 2 consecutive samples that have no results returned. After a third non-returned set of results, the sponsored centre may be suspended from the IEQAS program unless they provide valid explanations for their non-response.

COMPLAINTS AND APPEALS

Any complaint about the WFH IEQAS program will be treated as serious and will be dealt with as soon as possible by the director or manager. If a centre wishes to appeal the scoring they have received, they can contact IEQAS as below.

Address for complaints:

Dr. S. Kitchen
WFH IEQAS Program Director
3rd Floor, Pegasus House, 463A Glossop Road, Sheffield S10 2QD, U.K.
Tel: +44 (0)114 267 3300 E-mail: neqas@coageqa.org.uk

Or

Mirna Henin
WFH IEQAS Program Coordinator
1184 rue Sainte-Catherine Ouest, Bureau 500 Montréal, Québec H3B 1K1 Canada
Tel +1 514 875 7944 Email: ieqas@wfh.org

RESOURCES

In addition to an advisory role for individual laboratories WFH IEQAS and UK NEQAS BC also publishes and presents data through a variety of leading journals and meetings. An IEQAS participant's meeting is being held biennially as part of the WFH World Congress.

The WFH Diagnosis of Hemophilia and Other Bleeding Disorders: A Laboratory Manual 3rd edition) is available for free on the WFH eLearning platform along with hundreds of other resources. The Laboratory Manual is currently available in English, French and Spanish, with additional translations coming soon. Click here to view the laboratory manual

Visit the WFH Guidelines for the Management of Hemophilia Resource Hub to find narrated videos, key messages, and more. Click here to visit the resource hub.

PUBLICATIONS

Lack of grading agreement among international hemostasis external quality assessment programs.

Olson JD, Jennings I, Meijer P, Bon C, Bonar R, Favaloro EJ, Higgins RA, Keeney M, Mammen J, Marlar RA, Meley R, Nair SC, Nichols WL, Raby A, Reverter JC, Srivastava A, Walker I. Blood Coagul Fibrinolysis. 2018 Jan;29(1):111-119.

Towards harmonization of external quality assessment/proficiency testing in hemostasis. Favaloro EJ, Jennings I, Olson J, Van Cott EM, Bonar R, Gosselin R, Meijer P.Clin Chem Lab Med. 2018 Dec 19;57(1):115-126. doi: 10.1515/cclm-2018-0077.

Recent initiatives in harmonization of hemostasis practice. Favaloro EJ, Gosselin R, Olson J, Jennings I, Lippi G.Clin Chem Lab Med. 2018 Sep 25;56(10):1608-1619. doi: 10.1515/cclm-2018-0082.

Differential sensitivity of von Willebrand factor activity assays to reduced VWF molecular weight forms: A large international cross-laboratory study. Favaloro EJ, Bonar R, Hollestelle MJ, Jennings I, Mohammed S, Meijer P, Woods T, Meiring M.Thromb Res. 2018 Jun;166:96-105. doi: 10.1016/j.thromres.2018.04.015. Epub 2018 Apr 19.

The importance of commutability in material used for quality control purposes. Jennings I, Kitchen D, Kitchen S, Woods T, Walker I.Int J Lab Hematol. 2019 Feb;41(1):39-45. doi: 10.1111/ijlh.12918. Epub 2018 Sep 5.

Clotting and chromogenic factor VIII assay variability in post-infusion and spiked samples containing full-length recombinant FVIII or recombinant factor VIII Fc fusion protein (rFVIIIFc). Kitchen S, Jennings I, Makris M, Kitchen DP, Woods TAL, Walker ID.Int J Lab Hematol. 2019 Apr;41(2):176-183. doi: 10.1111/ijlh.12940. Epub 2018 Dec 17.

Performance of factor IX extended half-life product measurements in external quality control assessment programs. Nederlof A, Kitchen S, Meijer P, Cnossen M, Ali Pour N, Kershaw G, Jennings I, Walker I, de Maat MPM.J Thromb Haemost. 2020 Aug;18(8):1874-1883. doi: 10.1111/jth.14847. Epub 2020 Jun 10.

Effects of Emicizumab on APTT, FVIII assays and FVIII Inhibitor assays using different reagents: Results of a UK NEQAS proficiency testing exercise. Lowe A, Kitchen S, Jennings I, Kitchen DP, Woods TAL, Walker ID.Haemophilia. 2020 Nov;26(6):1087-1091. doi: 10.1111/hae.14177. Epub 2020 Oct 23.

Pre-analytical variables in haemostasis: Findings from the United Kingdom National External Quality Assessment scheme for Blood Coagulation (UK NEQAS BC) haemolysis exercise. Brown L, Jennings I, Kitchen S, Kitchen DP, Woods TAL, Walker ID.Int J Lab Hematol. 2021 Oct;43(5):1198-1206. doi: 10.1111/ijlh.13468. Epub 2021 Feb 19

Factor VIII/IX inhibitor testing practices in the United Kingdom: Results of a UKHCDO and UKNEQAS national survey. Batty P, Riddell A, Kitchen S, Sardo Infirri S, Walker I, Woods T, Jennings I, Hart DP.Haemophilia. 2021 May;27(3):490-499. doi: 10.1111/hae.14158. Epub 2021 Mar 2.

External quality assessment for one-stage and chromogenic factor IX assays in samples containing Alprolix (rFIXFc) or Idelvion (rIX-FP) and evidence that UK National External Quality Assessment Scheme for blood coagulation samples are commutable with patient samples. Kitchen S, Bowyer A, Lowe A, Jennings I, Walker ID.Int J Lab Hematol. 2022 Jun;44(3):619-625. doi: 10.1111/ijlh.13795. Epub 2022 Jan 17.

External Quality Assessment Data for Investigation of von Willebrand Disease: Focus on Relative Utility of Contemporary Functional von Willebrand Factor Assays. The United Kingdom National External Quality Assessment Scheme (UK NEQAS) Experience. Jennings I, Reilly-Stitt C, Lowe A, Kitchen S, Walker I.Semin Thromb Hemost. 2022 Sep;48(6):732-738. doi: 10.1055/s-0042-1753512. Epub 2022 Sep 2.

Internal Quality Control in Hemostasis Assays. Reilly-Stitt C, Jennings I, Kitchen S, Walker ID.Semin Thromb Hemost. 2023 Sep 25. doi: 10.1055/s-0043-1774381.

Practical handling of hemolytic, icteric and lipemic samples for coagulation testing in European laboratories. A collaborative survey from the European Organisation for External Quality Assurance Providers in Laboratory Medicine (EQALM). Kristoffersen AH, Hollestelle MJ, Cadamuro J, Hillarp A, Jennings I, Marrington R, Gidske G, Kesseler D, Meijer P. Clin Chem Lab Med. 2025 May 22. doi: 10.1515/cclm-2025-0319. Epub ahead of print. PMID: 40418797.

Reilly-Stitt C, Jennings I, Williams A, Kitchen S, Aiken L, Platton S, Raheja P, Lester W. UKNEQAS Blood Coagulation Factor Nine (FIX) Gene Therapy Supplementary Exercise 2025. Haemophilia. 2025 Sep 29. doi: 10.1111/hae.70138. Epub ahead of print. PMID: 41020323.

Jennings I, Baker P, Bowyer A, Crossette-Thambiah C, Gomez K, Lester W. Reporting haemostasis assays in IU/dL-A recommendation for harmonisation from the British Society for Haematology Haemostasis and Thrombosis Task Force, UK NEQAS for Blood Coagulation and the UK Haemophilia Centres Doctors Organisation. Br J Haematol. 2025 Oct;207(4):1698-1701. doi: 10.1111/bjh.70003. Epub 2025 Jul 16. PMID: 41070683.

The IEQAS Program is supported by funding from the Novo Nordisk Haemophilia Foundation